```
=> d his

     (FILE 'HOME' ENTERED AT 10:53:14 ON 08 AUG 2007)

     FILE 'REGISTRY' ENTERED AT 10:53:40 ON 08 AUG 2007
L1               STRUCTURE UPLOADED
L2           57881 S N2CNC/ESS (S) C6/ESS
L3               0 S L1 SAM SUB=L2
L4               0 S L1 SSS FULL SUB=L2
L5            6863 S N2CNC/ESS (S) NC2NC2/ESS
L6               1 S L1
L7              11 S L1 SAM SUB=L5
L8             184 S L1 SSS FULL SUB=L5

     FILE 'CAPLUS' ENTERED AT 10:55:46 ON 08 AUG 2007
L9             112 S L8
L10              2 S US200!-540283/APPS
L11            111 S L9 NOT L10

     FILE 'REGISTRY' ENTERED AT 10:57:19 ON 08 AUG 2007

=> d l1
L1 HAS NO ANSWERS
L1                STR
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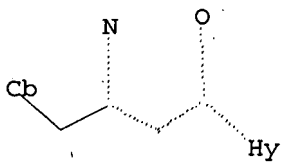

Structure attributes must be viewed using STN Express query preparation.

L10 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:565099 CAPLUS
DN 141:123655
TI Preparation of 3-amino-4-phenylbutanoic acid derivatives as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes
IN Duffy, Joseph L.; Edmondson, Scott D.; Kim, Dooseop; Kirk, Brian A.; Wang, Liping; Weber, Ann E.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058266	A1	20040715	WO 2003-US40114	20031216
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2508947	A1	20040715	CA 2003-2508947	20031216
	AU 2003297219	A1	20040722	AU 2003-297219	20031216
	EP 1583534	A1	20051012	EP 2003-814066	20031216
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
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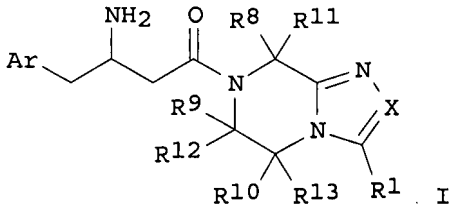
	US 2006052382	A1	20060309	US 2005-540283	20050620 <--
PRAI	US 2002-435389P	P	20021220		
	US 2003-469315P	P	20030509		
	WO 2003-US40114	W	20031216		

OS MARPAT 141:123655
GI



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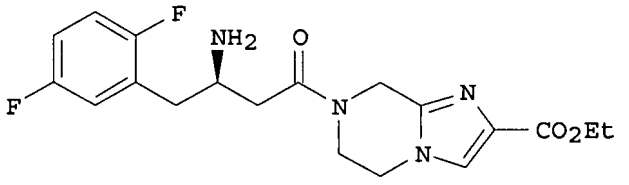
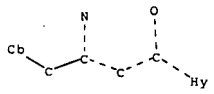


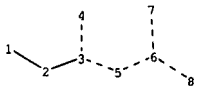
II

AB Title compds. I [wherein X = N or CR2; Ar = (un)substituted Ph; R1, R2 = independently H, halo, HO, cyano, (un)substituted alkyl(thio), alkoxy, etc.; R8-R10 = independently H, cyano, carboxy, (un)substituted (cyclo)alkyl, (hetero)aryl, etc.; R11-R13 = independently H, alkyl; with proviso; and pharmaceutically acceptable salts thereof] were prepared as

dipeptidyl peptidase inhibitors (no data). For example, Et 7-[(3R)-3-amino-4-(2,5-difluorophenyl)butanoyl]-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxylic acid trifluoroacetic acid salt (II•CF3CO2H) was given in a multiple-step synthesis starting from Et imidazo[1,2-a]pyrazine-2-carboxylate. Thus, I and their pharmaceutical compns. are useful for the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes (no data).

C:\Program Files\Stnexp\Queries\10540283-broad.str





chain nodes :
1 2 3 4 5 6 7 8
chain bonds :
1-2 2-3 3-4 3-5 5-6 6-7 6-8
exact/norm bonds :
1-2 2-3 3-4 3-5 5-6 6-7 6-8

Match level :
1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 7:CLASS 8:Atom
Generic attributes :
1:
Saturation : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic
8:
Saturation : Unsaturated
Type of Ring System : Polycyclic

Element Count :
Node 1: Limited
C,C6

Node 8: Limited
N,N4
C,C5

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:X

LOGINID:ssptasjl1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1          Web Page for STN Seminar Schedule - N. America
 NEWS  2  MAY 01  New CAS web site launched
 NEWS  3  MAY 08  CA/CAplus Indian patent publication number format defined
 NEWS  4  MAY 14  RDISCLOSURE on STN Easy enhanced with new search and display
                  fields
 NEWS  5  MAY 21  BIOSIS reloaded and enhanced with archival data
 NEWS  6  MAY 21  TOXCENTER enhanced with BIOSIS reload
 NEWS  7  MAY 21  CA/CAplus enhanced with additional kind codes for German
                  patents
 NEWS  8  MAY 22  CA/CAplus enhanced with IPC reclassification in Japanese
                  patents
 NEWS  9  JUN 27  CA/CAplus enhanced with pre-1967 CAS Registry Numbers
 NEWS 10  JUN 29  STN Viewer now available
 NEWS 11  JUN 29  STN Express, Version 8.2, now available
 NEWS 12  JUL 02  LEMBASE coverage updated
 NEWS 13  JUL 02  LMEDLINE coverage updated
 NEWS 14  JUL 02  SCISEARCH enhanced with complete author names
 NEWS 15  JUL 02  CHEMCATS accession numbers revised
 NEWS 16  JUL 02  CA/CAplus enhanced with utility model patents from China
 NEWS 17  JUL 16  CAplus enhanced with French and German abstracts
 NEWS 18  JUL 18  CA/CAplus patent coverage enhanced
 NEWS 19  JUL 26  USPATFULL/USPAT2 enhanced with IPC reclassification
 NEWS 20  JUL 30  USGENE now available on STN
 NEWS 21  AUG 06  CAS REGISTRY enhanced with new experimental property tags
 NEWS 22  AUG 06  BEILSTEIN updated with new compounds
 NEWS 23  AUG 06  FSTA enhanced with new thesaurus edition

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8

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specific topic.

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  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.
```



```
* * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 10:53:14 ON 08 AUG 2007

=> fil reg
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 10:53:40 ON 08 AUG 2007
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STRUCTURE FILE UPDATES:    7 AUG 2007  HIGHEST RN 944239-85-4
DICTIONARY FILE UPDATES:   7 AUG 2007  HIGHEST RN 944239-85-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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Uploading C:\Program Files\Stnexp\Queries\10540283-broad.str
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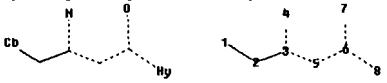


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chain nodes :
1  2  3  4  5  6  7  8
chain bonds :
1-2  2-3  3-4  3-5  5-6  6-7  6-8
exact/norm bonds :
1-2  2-3  3-4  3-5  5-6  6-7  6-8


Match level :
1:Atom  2:CLASS  3:CLASS  4:CLASS  5:CLASS  6:CLASS  7:CLASS  8:Atom
Generic attributes :
1:
Saturation             : Unsaturated
Number of Carbon Atoms : less than 7
Type of Ring System    : Monocyclic
```



```
8:
Saturation             : Unsaturated
Type of Ring System    : Polycyclic

Element Count :
Node 1: Limited
    C,C6

Node 8: Limited
    N,N4
    C,C5



L1      STRUCTURE UPLOADED

=> s n2cnc/ess (s) c6/ess
        786603 N2CNC/ESS
      24248219 C6/ESS
L2       57881 N2CNC/ESS (S) C6/ESS

=> s l1 sub=l2 sam
SAMPLE SUBSET SEARCH INITIATED 10:54:11 FILE 'REGISTRY'
SAMPLE SUBSET SCREEN SEARCH COMPLETED -        3 TO ITERATE

100.0% PROCESSED         3 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

PROJECTIONS (WITHIN SPECIFIED SUBSET):          ONLINE  **COMPLETE**
PROJECTED ITERATIONS (WITHIN SPECIFIED SUBSET):       3 TO       163
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET):          0 TO         0

L3             0 SEA SUB=L2 SSS SAM L1

=> s l1 sub=l2 sss full
FULL SUBSET SEARCH INITIATED 10:54:18 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -       66 TO ITERATE

100.0% PROCESSED        66 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

L4             0 SEA SUB=L2 SSS FUL L1

=> s n2cnc/ess (s) nc2nc2/ess
        786603 N2CNC/ESS
       1277691 NC2NC2/ESS
L5        6863 N2CNC/ESS (S) NC2NC2/ESS

=> s l1
SAMPLE SEARCH INITIATED 10:55:13 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -    63558 TO ITERATE

  3.1% PROCESSED      2000 ITERATIONS                             1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
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```
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:      1256139 TO  1286181
PROJECTED ANSWERS:             297 TO      973

L6             1 SEA SSS SAM L1

=> s l1 sub=l5 sam
SAMPLE SUBSET SEARCH INITIATED 10:55:23 FILE 'REGISTRY'
SAMPLE SUBSET SCREEN SEARCH COMPLETED -       21 TO ITERATE

100.0% PROCESSED        21 ITERATIONS                             11 ANSWERS
SEARCH TIME: 00.00.01

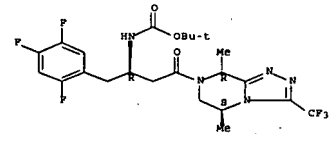
PROJECTIONS (WITHIN SPECIFIED SUBSET):          ONLINE  **COMPLETE**
PROJECTED ITERATIONS (WITHIN SPECIFIED SUBSET):     146 TO       694
PROJECTED ANSWERS (WITHIN SPECIFIED SUBSET):         22 TO       418

L7            11 SEA SUB=L5 SSS SAM L1

=> d scan

L7   11 ANSWERS   REGISTRY  COPYRIGHT 2007 ACS on STN
IN   Carbamic acid, [(1R)-3-[(5S,8R)-5,6-dihydro-5,8-dimethyl-3-
     (trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-
     trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI)
MF   C23 H27 F6 N5 O3

Absolute stereochemistry.
```

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l1 sub=l5 sss full
FULL SUBSET SEARCH INITIATED 10:55:41 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -      329 TO ITERATE

100.0% PROCESSED      329 ITERATIONS                            184 ANSWERS
SEARCH TIME: 00.00.01

L8           184 SEA SUB=L5 SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
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	ENTRY	SESSION
FULL ESTIMATED COST	364.90	365.11

FILE 'CAPLUS' ENTERED AT 10:55:46 ON 08 AUG 2007
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FILE COVERS 1907 - 8 Aug 2007 VOL 147 ISS 7
FILE LAST UPDATED: 7 Aug 2007 (20070807/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> s l8
L9          112 L8

=> s us200!-540283/apps
             1 US200!-540283/AP
             1 US200!-540283/PRN
L10          2 US200!-540283/APPS
               (US200!-540283/AP,PRN)

=> d l10 bib abs

L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
AN   2004:565099  CAPLUS  Full-text
DN   141:123655
TI   Preparation of 3-amino-4-phenylbutanoic acid derivatives as dipeptidyl
     peptidase inhibitors for the treatment or prevention of diabetes
IN   Duffy, Joseph L.; Edmondson, Scott D.; Kim, Dooseop; Kirk, Brian A.; Wang,
     Liping; Weber, Ann E.
PA   Merck & Co., Inc., USA
SO   PCT Int. Appl., 118 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   WO 2004058266       A1     20040715    WO 2003-US40114        20031216
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
```



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         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
             TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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     AU 2003297219       A1    20040722    AU 2003-297219         20031216
     EP 1583534          A1    20051012    EP 2003-814066         20031216
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2006513265       T     20060420    JP 2005-509979         20031216
     US 2006052382       A1    20060309    US 2005-540283         20050620 <--
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OS   MARPAT 141:123655
GI
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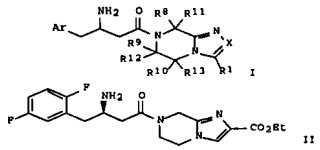

I

II

AB Title compds. I (wherein X = N or CR2; Ar = (un)substituted Ph; R1, R2 = independently H, halo, HO, cyano, (un)substituted alkyl(thio), alkoxy, etc.; R8-R10 = independently H, cyano, carboxy, (un)substituted (cyclo)alkyl, (hetero)aryl, etc.; R11-R13 = independently H, alkyl; with proviso; and pharmaceutically acceptable salts thereof] were prepared as dipeptidyl peptidase inhibitors (no data). For example, Et 7-[(3R)-3-amino-4-(2,5-difluorophenyl)butanoyl]-5,6,7,8- tetrahydroimidazo[1,2-a]pyrazine-2-carboxylic acid trifluoroacetic acid salt (II•CF3CO2H) was given in a multiple-step synthesis starting from Et imidazo[1,2-a]pyrazine-2-carboxylate. Thus, I and their pharmaceutical compns. are useful for the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as diabetes and particularly type 2 diabetes (no data).

```
=> s l9 not l10
L11         111 L9 NOT L10

=> fil reg
```

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.26	373.37

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.78	-0.78

FILE 'REGISTRY' ENTERED AT 10:57:19 ON 08 AUG 2007
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STRUCTURE FILE UPDATES: 7 AUG 2007 HIGHEST RN 944239-85-4
DICTIONARY FILE UPDATES: 7 AUG 2007 HIGHEST RN 944239-85-4

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TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

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http://www.cas.org/support/stngen/stndoc/properties.html

```
=> d his

     (FILE 'HOME' ENTERED AT 10:53:14 ON 08 AUG 2007)

     FILE 'REGISTRY' ENTERED AT 10:53:40 ON 08 AUG 2007
L1             STRUCTURE UPLOADED
L2         57881 S N2CNC/ESS (S) C6/ESS
L3             0 S L1 SAM SUB=L2
L4             0 S L1 SSS FULL SUB=L2
L5          6863 S N2CNC/ESS (S) NC2NC2/ESS
L6             1 S L1
L7            11 S L1 SAM SUB=L5
L8           184 S L1 SSS FULL SUB=L5

     FILE 'CAPLUS' ENTERED AT 10:55:46 ON 08 AUG 2007
L9           112 S L8
L10            2 S US200!-540283/APPS
L11          111 S L9 NOT L10

     FILE 'REGISTRY' ENTERED AT 10:57:19 ON 08 AUG 2007

=> d l1
L1 HAS NO ANSWERS
L1             STR
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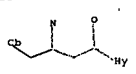

Structure attributes must be viewed using STN Express query preparation.

```
=> fil caplus
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.45	373.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.78

FILE 'CAPLUS' ENTERED AT 10:57:51 ON 08 AUG 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 8 Aug 2007 VOL 147 ISS 7
FILE LAST UPDATED: 7 Aug 2007 (20070807/ED)

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http://www.cas.org/infopolicy.html

```
=> d his

     (FILE 'HOME' ENTERED AT 10:53:14 ON 08 AUG 2007)

     FILE 'REGISTRY' ENTERED AT 10:53:40 ON 08 AUG 2007
L1             STRUCTURE UPLOADED
L2         57881 S N2CNC/ESS (S) C6/ESS
L3             0 S L1 SAM SUB=L2
L4             0 S L1 SSS FULL SUB=L2
L5          6863 S N2CNC/ESS (S) NC2NC2/ESS
L6             1 S L1
L7            11 S L1 SAM SUB=L5
L8           184 S L1 SSS FULL SUB=L5

     FILE 'CAPLUS' ENTERED AT 10:55:46 ON 08 AUG 2007
L9           112 S L8
L10            2 S US200!-540283/APPS
L11          111 S L9 NOT L10

     FILE 'REGISTRY' ENTERED AT 10:57:19 ON 08 AUG 2007

     FILE 'CAPLUS' ENTERED AT 10:57:51 ON 08 AUG 2007

=> d l11 tot bib abs hitstr
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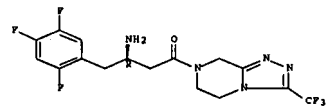
THE ESTIMATED COST FOR THIS REQUEST IS 584.97 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L11 ANSWER 1 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:770084 CAPLUS Full-text
DN 147:110561
TI Efficacy and safety of incretin therapy in type 2 diabetes. Systematic review and meta-analysis
AU Amori, Renee E.; Lau, Joseph; Pittas, Anastassios G.
CS Division of Endocrinology, Diabetes and Metabolism, Tufts-New England Medical Center, Boston, MA, USA
SO JAMA, the Journal of the American Medical Association (2007), 298(2), 194-206
CODEN: JAMAAP; ISSN: 0098-7484
PB American Medical Association
DT Journal
LA English
AB Context Pharmacotherapies that augment the incretin pathway have recently become available, but their role in the management of type 2 diabetes is not well defined. Objective To assess the efficacy and safety of incretin-based therapy in adults with type 2 diabetes based on randomized controlled trials published in peer-reviewed journals or as abstrs. Data Sources We searched MEDLINE (1966-May 20,2007) and the Cochrane Central Register of Controlled Trials (second quarter, 2007) for English-language randomized controlled trials involving an incretin mimetic (glucagonlike peptide 1 [GLP-1] analog) or enhancer (dipeptidyl peptidase 4 [DPP4] inhibitor). We also searched prescribing information, relevant Web sites, reference lists and citation sections of recovered articles, and abstrs. presented at recent conferences. Study Selection Randomized controlled trials were selected if they were at least 12 wk in duration, compared incretin therapy with placebo or other diabetes medication, and reported Hb Alc data in nonpregnant adults with type 2 diabetes. Data Extraction Two reviewers independently assessed trials for inclusion and extracted data. Differences were resolved by consensus. Meta-analyses were conducted for several efficacy and safety outcomes. Results Of 355 potentially relevant articles identified, 51 were retrieved for detailed evaluation and 29 met the inclusion criteria. Incretins lowered Hb A, compared with placebo (weighted mean difference, -0.97% [95% confidence interval {CI}, -1.13% to-0.81%] for GLP-1 analogs and -0.74% [95% CI, -0.85% to-0.62%] for DPP4 inhibitors) and were noninferior to other hypoglycemic agents. Glucagon-like peptide 1 analogs resulted in weight loss (1.4 kg and 4.8 kg vs. placebo and insulin, resp.) while DPP4 inhibitors were weight neutral. Glucagonlike peptide 1 analogs had more gastrointestinal side effects (risk ratio, 2.9 [95% CI, 2.0-4.2] for nausea and 3.2 [95% CI, 2.5-4.4] for vomiting). Dipeptidyl peptidase 4 inhibitors had an increased risk of infection (risk ratio, 1.2 [95% CI, 1.0-1.4] for nasopharyngitis and 1.5 [95% CI, 1.0-2.2] for urinary tract infection) and headache (risk ratio, 1.4 [95% CI, 1.1-1.7]). All but 3 trials had a 30-wk or shorter duration; thus, long-term efficacy and safety could not be evaluated. Conclusions Incretin therapy offers an alternative option to currently available hypoglycemic agents for nonpregnant adults with type 2 diabetes, with modest efficacy and a favorable weight-change profile. Careful postmarketing surveillance for adverse effects, especially among the DPP4 inhibitors, and continued evaluation in longer-term studies and in clin. practice are required to determine the role of this new class among current pharmacotherapies for type 2 diabetes.
IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and safety of incretin therapy in type 2 diabetes. systematic review and meta-anal.)
RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 2 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:762624 CAPLUS Full-text
DN 147:150836
TI Pharmaceutical compositions of combinations of dipeptidyl peptidase-4 inhibitors with metformin
IN Kamali, Ashkan; Alani, Laman; Fliszar, Kyle A.; Ghosh, Soumojeet; Tijerina, Monica
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 19pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

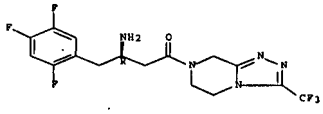
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007078726	A2	20070712	WO 2006-US47380	20061212

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-750954P P 20051216
AB Disclosed are pharmaceutical compns. comprising fixed-dose combinations of a dipeptidyl peptidase-4 inhibitor and metformin, methods of preparing such pharmaceutical compns., and methods of treating Type 2 diabetes with such pharmaceutical compns. For example, a coated tablet was prepared by wet granulation from sitagliptin phosphate monohydrate 64.25, metformin hydrochloride 500, polyvinylpyrrolidone 48.2, sodium lauryl sulfate 3.45, microcryst. cellulose (Avicel PH-102), sodium stearyl fumarate 13.8, water q.s., and coating material (Opadry II) 17.2 mg..
IT 486460-32-6, Sitagliptin 654671-77-9 654671-78-0
, Sitagliptin phosphate
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. of combinations of dipeptidyl peptidase-4

inhibitors with metformin)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

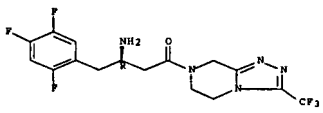


RN 654671-77-9 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

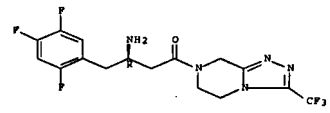
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1)

(CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 3 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:652182 CAPLUS Full-text
TI Docking-based 3D-QSAR study for selectivity of DPP4, DPP8, and DPP9 inhibitors
AU Kang, Nam Sook; Ahn, Jin Hee; Kim, Sung Soo; Chae, Chong Hak; Yoo, Sung-Eun
CS Korea Research Institute of Chemical Technology, Daejeon, 305-600, S. Korea
SO Bioorganic & Medicinal Chemistry Letters (2007), 17(13), 3716-3721
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
AB In order to obtain information regarding the design of selective DPP4 inhibitors, a 3D-QSAR study was conducted using DPP4, DPP8, and DPP9 inhibitors including newly synthesized six- and seven-membered cyclic hydrazine derivs. (KR64300, KR64301), which were evaluated in vitro for their inhibition of DPP4, DPP8, and DPP9. In this study, a highly predictive CoMFA model based on the fast-docking for DPP4, DPP8, and DPP9 inhibitors was obtained. This reliable model showed leave-one-out cross-validation q2 and conventional r2 values of 0.68 and 0.96 for the DPP4 inhibitors, 0.58 and 0.98 for the DPP8 inhibitors, and 0.68 and 0.97 for the DPP9 inhibitors, resp. The validation of the CoMFA model was confirmed by the compds. in the test set,

including the synthesized six- and seven-membered cyclic hydrazines. According to this study, to obtain selective DPP4 inhibitors compared to their isoenzymes, the interaction of the inhibitors with the S3 site and S1' site in DPP4 must be considered. The proposed newly synthesized compds., KR64300 and KR64301, interact well with the sites mentioned above, showing excellent selectivity.

IT INDEXING IN PROGRESS

IT 654671-78-0, MK-0431

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PRP (Properties); USES (Uses)

(docking-based 3D-QSAR study for selectivity of DPP4, DPP8, and DPP9 inhibitors)

RN 654671-78-0 CAPLUS

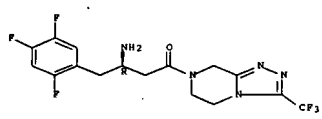
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6

CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2

CMF H3 O4 P

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:602614 CAPLUS Full-text

TI Rational design of a novel, potent, and orally bioavailable cyclohexylamine DPP-4 inhibitor by application of molecular modeling and X-ray crystallography of sitagliptin

AU Biftu, Tesfaye; Scapin, Giovanna; Singh, Suresh; Feng, Dennis; Becker, Joe W.; Eiermann, George; He, Huaibing; Lyons, Kathy; Patel, Sangita; Petrov, Aleksandr; Sinha-Roy, Ranabir; Zhang, Bei; Wu, Joseph; Zhang, Xiaoping; Doss, George A.; Thornberry, Nancy A.; Weber, Ann E.

CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck & Co., Inc., Rahway, NJ, 07065, USA

SO Bioorganic & Medicinal Chemistry Letters (2007), 17(12), 3384-3387
CODEN: BMCLE8; ISSN: 0960-894X

PB Elsevier Ltd.

DT Journal

LA English

AB Mol. modeling was used to design a rigid analog of sitagliptin 1. The x-ray crystal structure of sitagliptin bound to DPP-4 suggested that the central β-amino Bu amide moiety could be replaced with a cyclohexylamine group. This was confirmed by structural anal. and the resulting analog (I) was synthesized and a potent DPP-4 inhibitor (IC50 = 21 nM) with excellent in vivo activity and pharmacokinetic profile.

IT INDEXING IN PROGRESS

IT 486460-32-6, Sitagliptin

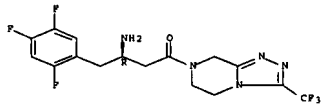
RL: PAC (Pharmacological activity); BIOL (Biological study)

(rational design of a novel, potent, and orally bioavailable cyclohexylamine DPP-4 inhibitor by application of mol. modeling and X-ray crystallog. of sitagliptin)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:589017 CAPLUS Full-text

DN 147:64628

TI DDPIV inhibitors

AU Yamada, Yuichiro

CS Sch. of Medicine, Akita Univ., Japan

SO Igaku no Ayumi (2007), 220(13), 1219-1222
CODEN: IGAYAY; ISSN: 0039-2359

PB Ishiyaku Shuppan

DT Journal; General Review

LA Japanese

AB A review on effects of DDPIV inhibitors on insulin secretion and their application for diabetes treatment.

IT 486460-32-6, Sitagliptin

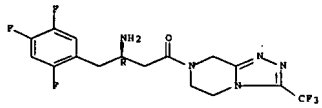
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(application of DDPIV inhibitors on diabetes treatment)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 6 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:554954 CAPLUS Full-text

DN 147:86058

TI Dipeptidyl peptidase-4 inhibitors for the treatment of type 2 diabetes: focus on sitagliptin

AU Herman, G. A.; Stein, P. P.; Thornberry, N. A.; Wagner, J. A.

CS Merck Research Laboratories, Rahway, NJ, USA

SO Clinical Pharmacology & Therapeutics (New York, NY, United States) (2007), 81(5), 761-767
CODEN: CLPTAT; ISSN: 0009-9236

PB Nature Publishing Group

DT Journal; General Review

LA English

AB A review. Dipeptidyl peptidase-4 (DPP-4) inhibitors represent a new class of oral antihyperglycemic agents to treat patients with type 2 diabetes. DPP-4 inhibitors improve fasting and postprandial glycemic control without hypoglycemia or weight gain. This article focuses on the physiol., clin. pharmacol., tolerability, and clin. utility of the DPP-4 inhibitor sitagliptin in the management of type 2 diabetes.

IT 486460-32-6, Sitagliptin

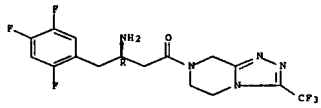
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(dipeptidyl peptidase 4 inhibitor, sitagliptin for treatment of type 2 diabetes)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:553808 CAPLUS Full-text

DN 146:474633

TI Discovery of JANUVIA (sitagliptin), a selective dipeptidyl peptidase IV inhibitor for the treatment of type 2 diabetes

AU Thornberry, Nancy A.; Weber, Ann E.

CS Departments of Metabolic Disorders and Medicinal Chemistry, Merck Research Laboratories, Rahway, NJ, 07065, USA

SO Current Topics in Medicinal Chemistry (Sharjah, United Arab Emirates) (2007), 7(6), 557-568
CODEN: CTMCCL; ISSN: 1568-0266

PB Bentham Science Publishers Ltd.

DT Journal; General Review

LA English

AB A review. The emergence of glucagon-like peptide 1 (GLP-1) as a well validated approach to the treatment of type 2 diabetes and preclin. validation of dipeptidyl peptidase IV (DPP-4) inhibition as an alternate, oral approach to GLP-1 therapy prompted the initiation of a DPP-4 inhibitor program at Merck in 1999. DPP-4 inhibitors threo- and allo-isoleucyl thiazolidide were in-licensed to jump start the program; however, development was discontinued due to profound toxicity in rat and dog safety studies. The observation that both compds. inhibit the related proline peptidases DPP8 and DPP9 led to the hypothesis that inhibition of DPP8 and/or DPP9 could evoke severe toxicities in preclin. species. Indeed, the observed toxicities were recapitulated with a selective dual DPP8/9 inhibitor but not with an inhibitor selective for DPP-4. Thus, medicinal chemical efforts focused on identifying a highly selective DPP-4 inhibitor for clin. development. Initial work in an α-amino acid series related to isoleucyl thiazolidide was discontinued due to lack of selectivity; however, SAR studies on two screening leads led to the identification of a highly selective β-amino acid piperazine series. In an effort to stabilize the piperazine moiety, which was extensively metabolized in vivo, a series of bicyclic derivs. were prepared, culminating in the identification of a potent and selective triazolopiperazine series. Unlike their monocyclic counterparts, these analogs typically showed excellent pharmacokinetic properties in preclin. species. Optimization of this series led to the discovery of JANUVIA (sitagliptin), a highly selective DPP-4 inhibitor for the treatment of type 2 diabetes.

IT 654671-78-0, Januvia

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Januvia (sitagliptin), a selective dipeptidyl peptidase IV inhibitor for treatment of type 2 diabetes)

RN 654671-78-0 CAPLUS

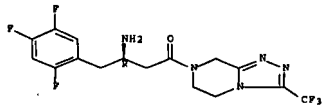
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6

CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:538695 CAPLUS Full-text
DN 146:521789
TI Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Cow, Christopher; Azimioara, Mihai; Russo, Ross; Xie, Yongping; Wang, Xing
PA IRM LLC, Bermuda
SO PCT Int. Appl., 139pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056366	A2	20070518	WO 2006-US43342	20061107
WO 2007056366	A3	20070705		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRAI US 2005-734683P P 20051107

OS MARPAT 146:521789
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ. In compds. I, W is O or S; R1 is -L1-X-C(R7R8)-L2-CO2R9; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R7 and R8 are independently H, C1-4 alkyl, or C1-4 alkoxy; R9 is H or C1-6 alkyl; p is 0-3; each R2 is independently selected from halo, C1-6 alkyl, C2-6 alkenyl, C1-4 alkoxy, C1-4 alkylthio, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; n is 0-3; R3 and R4 are independently H or C1-6 alkyl; R5 and R6 are independently selected from H, C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl; Y is O, S, NR10, or CR10R11; Z is C10R11 or S; and R10 and R11 are independently selected from H and C1-6 alkyl; including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from anti-diabetic agents, hypolipidemic agents, anti-obesity agents, anti-hypertensive agents, etc., as well as to the use of the compns. for the treatment or prevention of disease or disorders associated with PPAR activity. Regioselective acetylation of Et (2-methylphenoxy)acetate followed by Baeyer-Villiger oxidation, methanolysis, and regioselective bromination gave phenoxyacetate II, which underwent O-silylation, Suzuki coupling with cyclopropylboronic acid, and desilylation resulting in the formation of cyclopropylphenoxyacetate III. Substitution of 3-chloropropanol with potassium cyanide followed by sulfolysis to the thioamide and heterocyclization with 2-bromo-1-(4-trifluoromethylphenyl)ethanone formed thiazole IV, which was coupled to III under Mitsunobu conditions and hydrolyzed to give thiazole V. The compds. of the invention, e.g., V, are modulators of PPAR, particularly PPARδ (no data).

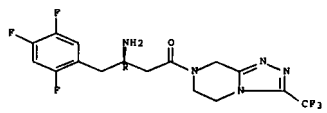
IT 654671-78-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of oxazole and thiazole compds. as PPAR modulators)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 9 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:538194 CAPLUS Full-text
DN 146:521786
TI Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Cow, Christopher; Azimioara, Mihai; Russo, Ross
PA IRM LLC, Bermuda
SO PCT Int. Appl., 62pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056496	A1	20070516	WO 2006-US43586	20061107

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-734678P P 20051107
OS MARPAT 146:521786
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ. In compds. I, W is O or S; R1 is -L1-X-C(R8R9)-L2-CO2R10; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R8 and R9 are independently H, C1-4 alkyl, or C1-4 alkoxy; R10 is H or C1-6 alkyl; p is 0-3; each R2 is independently selected from halo, C1-6 alkyl, C2-6 alkenyl, C1-4 alkoxy, C1-4 alkylthio, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; n is 0-3; R3 and R4 are independently H or C1-6 alkyl; R5 and R6 are independently selected from H, C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl; R7 is H, C1-6 alkyl, -L3-C6-12 aryl, -L3-C3-12 cycloalkyl, -L3-OR11, or -L3-N(R11R12); L3 is a bond or C1-4 alkylene; and R11 and R12 are independently H or C1-6 alkyl; including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from anti-diabetic agents, hypolipidemic agents, anti-obesity agents, anti-hypertensive agents, etc., as well as to the use of the compns. for the treatment or prevention of disease or disorders associated with PPAR activity. Regioselective bromination of 4-benzyloxyphenol followed by O-silylation, substitution with tetramethyltin, and desilylation gave 4-benzyloxy-2-methylphenol, which underwent substitution of Me 2-bromo-2-methylpropionate, debenzylation, and substitution of 1,2-dibromoethane resulting in the formation of ester II. Heterocyclization of 2-bromo-1-(4-trifluoromethylphenyl)ethanone with thiourea formed aminothiazole III, which underwent substitution of bromide II, N-methylation, and ester hydrolysis to give thiazole IV. The compds. of the invention, e.g., IV, are modulators of PPAR, particularly PPARδ (no data).

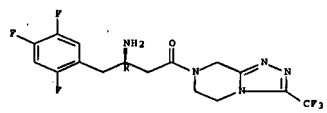
IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of oxazole and thiazole compds. as PPAR modulators)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

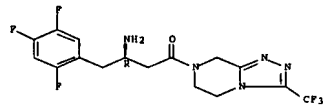
CRN 7664-38-2
CMF H3 O4 P

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:537237 CAPLUS Full-text
TI Dipeptidyl peptidase-4 inhibitors and the management of type 2 diabetes mellitus
AU Rosenstock, Julio; Zinman, Bernard
CS Dallas Diabetes and Endocrine Center at Medical City, Dallas, TX, USA
SO Current Opinion in Endocrinology, Diabetes and Obesity (2007), 14(2), 98-107
CODEN: COEDFK; ISSN: 1752-296X
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
AB Purpose of review: To review recent clin. trials of oral dipeptidyl peptidase-4 inhibitors and examine their role in managing type 2 diabetes mellitus. Recent findings: Oral dipeptidyl peptidase-4 inhibitors improve islet function by increasing α-cell and β-cell responsiveness to glucose, resulting in improved glucose-dependent insulin secretion and reduced inappropriate glucagon secretion. These agents appear to have physiol. based antihyperglycemic effects and may modify the progressive nature of type 2 diabetes mellitus. In clin. trials sitagliptin and vildagliptin have modest demonstrated effectiveness, with clin. meaningful redns. of glycated Hb when used as monotherapy. They appear promising in combination or added to ongoing therapy with other antidiabetic drugs (e.g. metformin, thiazolidinediones, or insulin). Dipeptidyl peptidase-4 inhibitors themselves are not associated with hypoglycemia or weight gain and appear to have a benign safety profile. Summary: Oral dipeptidyl peptidase-4 inhibitors may prove valuable in the treatment of diabetes, given their effectiveness in reducing glycated Hb with neutral weight effects and without the adverse events associated with other agents. Dipeptidyl peptidase-4 inhibitors appear to improve islet function and may modify the course of diabetes; this, however, must be confirmed with long-term controlled studies to demonstrate sustained glycemic control that translates into β-cell preservation.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sitagliptin showed redns. in glycated Hb in patient with type 2 diabetes mellitus)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-

a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

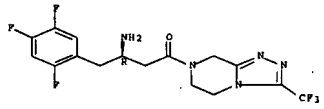
L11 ANSWER 11 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:536945 CAPLUS Full-text
DN 146:507832
TI Multi-stage process to control particle size of pharmaceutical substance
IN Mooney, Brett Antony
PA Alphapharm Pty. Ltd., Australia; Keramidas, Panagiotis
SO PCT Int. Appl., 27pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007053904	A1	20070510	WO 2006-AU1687	20061110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI AU 2005-906227	A	20051110		

AB This invention relates to multi-stage process to control the particle size of a pharmaceutical substance comprising the steps of: passing the pharmaceutical substance through a first stage of a particle size reduction process with a first set of particle size control parameters to obtain a feedstock of reduced median particle size and lesser distribution of median particle size for a second stage of a particle size reduction process; passing the feedstock, through a second stage of a particle size reduction process with a second set of particle size control parameters; optionally, using the product of the second stage or subsequent stages as a feedstock in further stages of a multi-stage particle size reduction process with a set of particle size control parameters for each stage; and collecting a pharmaceutical substance with a median particle size greater than 10μm and with a narrow, reproducible distribution of median particle sizes. Thus, oxcarbazepine was milled in a 12" spiral jet mill to produce particle size of 15μm to 17μm.

IT 486460-32-6, Sitagliptin
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multi-stage process to control particle size of pharmaceutical substance)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:536876 CAPLUS Full-text
DN 146:521785
TI Oxazoles and thiazoles as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Xie, Yongping; Wang, Xing; Russo, Ross; Cow, Christopher; Azimioara, Mihai
PA IRM LLC, Bermuda
SO PCT Int. Appl., 80pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007056497	A1	20070518	WO 2006-US43587	20061107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-734592P	P	20051107		

OS MARPAT 146:521785
GI

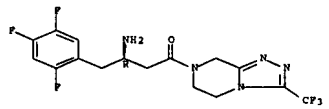
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazoles and thiazoles of formula I, which modulate the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ. In compds. I, W is N or CH; Y is O, S, CH2CH2, or CR5R6, where R5 and R6 are independently selected from H and C1-6 alkyl; Z is S or O; R1 is -L1-X-C(R7R8)-L2-CO2R9; L1 and L2 are independently a bond or C1-4 alkylene; X is a bond, O, or S; R7 and R8 are independently H, C1-4 alkyl, or C1-4 alkoxy, or R7 and R8, together with the carbon atom to which they are attached, form C3-12 cycloalkyl; R9 is H or C1-6 alkyl; n is 0-3; each R2 is independently selected from halo, C1-4 alkyl, C1-4 alkoxy, C1-4 alkylthio, and C3-12 cycloalkyl; R3 is C1-8 alkyl; and R4 is selected from halo, C1-4 alkyl, C1-4 haloalkyl, and C1-4 haloalkoxy; including salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of a compound I with one or more pharmaceutically acceptable excipients, optionally containing another active ingredient selected from anti-diabetic agents, hypolipidemic agents, anti-obesity agents, anti-hypertensive agents, etc., as well as to the use of the compns. for the treatment or prevention of disease or disorders associated with PPAR activity. Diazotization of 4- (trifluoromethoxy)acetophenone followed by heterocyclization with acetonitrile, and sequential double bromination gave dibromooxazole II. O-Benzylation of 4-hydroxybenzaldehyde, condensation with Et ethoxyacetate, and hydrogenation resulted in the formation of ethoxypropionate III, which underwent substitution of II followed by Suzuki coupling with 2-isopropoxy-5-pyrimidineboronic acid (two-step preparation from 5-bromo-2-chloropyrimidine is given) and ester hydrolysis to give oxazole IV. The compds. of the invention, e.g., IV, are modulators of PPAR, particularly PPARδ (no data).
IT 654671-78-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of oxazole and thiazole compds. as PPAR modulators)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



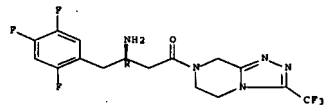
CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

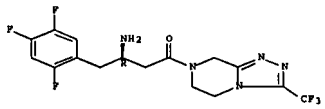
L11 ANSWER 13 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:531591 CAPLUS Full-text
DN 147:108754
TI DPP 4 inhibitor, sitagliptin
AU Okamoto, Taro; Nonaka, Kenji
CS Clinical Development Institute, Banyu Pharmaceutical co. Ltd., Japan
SO BIO Clinica ((2007)), 22(5), 430-435
CODEN: BCILCY; ISSN: 0919-8237
PB Hokuryukan
DT Journal; General Review
LA Japanese
AB A review. Sitagliptin, a kind of DPP 4 inhibitor, is reviewed in the aspects of its pharmacol. effect and clin. effect with 21 refs. Sitagliptin which is excellent elective DPP 4 inhibitor for type 2 diabetes mellitus patients is administrated once daily and shows effectiveness and good tolerance less side effect, such as hypoglycemia and weight gain. In vitro pharmacol. show that sitagliptin has at least of 2600 times DPP-4 elective margin comparing with DPP8, DPP9. In vivo pharmacol. over animal experiment show that number of islet β-cell of diabetes decreased by sitagliptin. At home and abroad by clin. phase I and II trial, sitagliptin shows effect of deceasing HbA1C level with safety so that the improved blood glucose control effect by sitagliptin is obvious.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DPP 4 inhibitor, sitagliptin)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 14 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:522129 CAPLUS Full-text
DN 147:132522
TI Sitagliptin
AU Lyseng-Williamson, Katherine A.
CS Wolters Kluwer Health/Adis, Auckland, N. Z.
SO Drugs ((2007)), 67(4), 587-597
CODEN: DRUGAY; ISSN: 0012-6667
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review. Sitagliptin, an oral dipeptidyl peptidase-4 (DPP-4) inhibitor, improves glycemic control by inhibiting DPP-4 inactivation of the incretin hormones glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide. This increases active incretin and insulin levels, and decreases glucagon levels and post-glucose-load glucose excursion. In large, well designed phase III trials in patients with type 2 diabetes mellitus, sitagliptin 100 or 200mg once daily alone or in combination with other antihyperglycemics was associated with significant improvements relative to placebo in overall glycemic control and indexes for insulin response and β-cell function. Improvements from baseline in mean glycosylated Hb (HbA1c) were significantly greater with sitagliptin monotherapy than with placebo in patients with type 2 diabetes. As add-on therapy in patients with suboptimal glycemic control despite oral antihyperglycemic treatment, sitagliptin improved HbA1c to a significantly greater extent than placebo when added to metformin or pioglitazone and was noninferior to glipizide when added to metformin. Sitagliptin was well tolerated when administered alone or in combination with other antihyperglycemics, with an adverse event profile similar to that shown with placebo. The incidence of hypoglycemia with sitagliptin was similar to that with placebo and, in combination with metformin, lower than that with glipizide. Sitagliptin had a generally neutral effect on bodyweight.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Januvia alone or in combination with antihyperglycemic improved overall glycemic control, insulin response and β-cell function in patient with type 2 diabetes mellitus)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

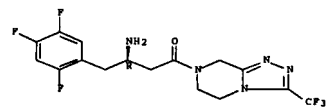
Absolute stereochemistry.



RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:513287 CAPLUS Full-text
DN 146:454126
TI Transport of the dipeptidyl peptidase-4 inhibitor sitagliptin by human organic anion transporter 3, organic anion transporting polypeptide 4C1, and multidrug resistance P-glycoprotein
AU Chu, Xiao-Yan; Bleasby, Kelly; Yabut, Jocelyn; Cai, Xiaoxin; Chan, Grace Hoyee; Hafey, Michael J.; Xu, Shiyao; Bergman, Arthur J.; Braun, Matthew P.; Dean, Dennis C.; Evers, Raymond
CS Department of Drug Metabolism, Merck and Co., Rahway, NJ, USA
SO Journal of Pharmacology and Experimental Therapeutics ((2007)), 321(2), 673-683
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Sitagliptin, a selective dipeptidyl peptidase 4 inhibitor recently approved for the treatment of type 2 diabetes, is excreted into the urine via active tubular secretion and glomerular filtration in humans. In this report, we demonstrate that sitagliptin is transported by human organic anion transporter hOAT3 (Km = 162 μM), organic anion transporting polypeptide OATP4C1, and multidrug resistance (MDR) P-glycoprotein (Pgp), but not by human organic cation transporter 2 hOCT2, hOAT1, oligopeptide transporter hPEPT1, OATP2B1, and the multidrug resistance proteins MRP2 and MRP4. Our studies suggested that hOAT3, OATP4C1, and MDR1 Pgp might play a role in transporting sitagliptin into and out of renal proximal tubule cells, resp. Sitagliptin did not inhibit hOAT1-mediated cidofovir uptake, but it showed weak inhibition of hOAT3-mediated cimetidine uptake (IC50 = 160 μM). HOAT3-mediated sitagliptin uptake was inhibited by probenecid, ibuprofen, furosemide, fenofibric acid, quinapril, indapamide, and cimetidine with IC50 values of 5.6, 3.7, 1.7, 2.2, 6.2, 11, and 79 μM, resp. Sitagliptin did not inhibit Pgp-mediated transport of digoxin, verapamil, ritonavir, quinidine, and vinblastine. Cyclosporine A significantly inhibited Pgp-mediated transport of sitagliptin (IC50 = 1 μM). Our data indicate that sitagliptin is unlikely to be a perpetrator of drug-drug interactions with Pgp, hOAT1, or hOAT3 substrates at clin. relevant concns. Renal secretion of sitagliptin could be inhibited if coadministered with OAT3 inhibitors such as probenecid. However, the magnitude of interactions should be low, and the effects may not be clin. meaningful, due to the high safety margin of sitagliptin.
IT 486460-32-6, Sitagliptin
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(transport of dipeptidyl peptidase-4 inhibitor sitagliptin by human transport proteins and possible drug interactions)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

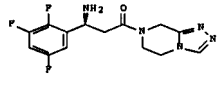


RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:485597 CAPLUS Full-text
DN 146:482092
TI Combination of a dipeptidyl peptidase-4 inhibitor and an anti-hypertensive agent for the treatment of diabetes and hypertension
IN Hasegawa, Philip A.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 42pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007050485	A2	20070503	WO 2006-US41233	20061020
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-730167P	P	20051025		

GI



I

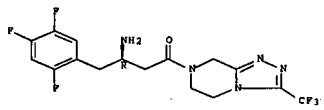
AB The invention relates to pharmaceutical compns. comprising a combination of a particular dipeptidyl peptidase-4 (DPP-4) inhibitor I and an anti-hypertensive agent selected from the group consisting of an angiotensin II receptor antagonist and an angiotensin converting enzyme inhibitor, kits containing such combinations and methods of using such compns. for the treatment of diabetes, diabetes-related disorders, hypertension, and hypertension-related disorders. Example compound I and I•H3PO4 was prepared by a multistep procedure (procedure given). Compound I and I•H3PO4 were evaluated for their DPP-4 inhibitory activity.
IT 486460-32-6P, Sitagliptin
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of sitagliptin phosphate and combination of particular DPP-4

inhibitor and antihypertensive agent selected from angiotensin II receptor antagonist and ACE inhibitor for treatment of diabetes and hypertension)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 654671-78-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of sitagliptin phosphate and combination of particular DPP-4 inhibitor and antihypertensive agent selected from angiotensin II receptor antagonist and ACE inhibitor for treatment of diabetes and hypertension)

RN 654671-78-0 CAPLUS

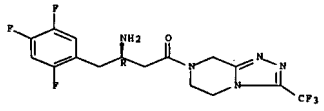
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6

CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2

CMF H3 O4 P

IT 767340-03-4P

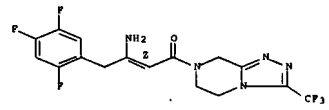
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of sitagliptin phosphate and combination of particular DPP-4 inhibitor and antihypertensive agent selected from angiotensin II receptor antagonist and ACE inhibitor for treatment of diabetes and hypertension)

RN 767340-03-4 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(2Z)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)-2-butenyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L1-1 ANSWER 31 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:438460 CAPLUS Full-text

DN 146:435216

TI Combinations and conjugates of dipeptidyl peptidase IV inhibitors and gastrins for treatment of disorders of metabolism and homeostasis

IN Cruz, Antonio

PA Waratah Pharmaceuticals, Inc., Can.

SO PCT Int. Appl., 64pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007041833	A1	20070419	WO 2006-CA1644	20061006

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-724919P P 20051007

OS MARPAT 146:435216

AB The invention relates to compns., conjugates, and methods for the prevention and/or treatment of a condition and/or disease comprising a therapeutically effective amount of a DPP-IV inhibitor and a gastrin compound The combination of a DPP-IV inhibitor and a gastrin compound provides beneficial effects, in particular sustained beneficial effects, in the prevention and/or treatment of conditions and/or diseases for which either a DPP-IV inhibitor or a gastrin compound have been demonstrated to have a therapeutic effect, including but not limited to diabetes, hypertension, chronic heart failure, fluid retentive states, obesity, metabolic syndrome and related diseases and disorders. Combinations of a DPP-IV inhibitor and a gastrin compound can be selected to provide unexpectedly additive effects or synergistic effects.

IT 486460-32-6D, Sitagliptin, conjugates with gastrin

654671-78-0D, MK 0431, conjugates with gastrin

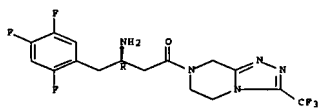
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combinations and conjugates of dipeptidyl peptidase IV inhibitors and gastrins for treatment of disorders of metabolism and homeostasis)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 654671-78-0 CAPLUS

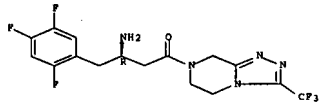
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6

CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2

CMF H3 O4 P

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1-1 ANSWER 32 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:417196 CAPLUS Full-text

DN 147:440

TI Sitagliptin: profile of a novel DPP-4 inhibitor for the treatment of type 2 diabetes

AU Gallwitz, Baptist

CS Department of Medicine IV, Eberhard-Karls-University, Tuebingen, Germany

SO Drugs of Today (2007), 43(1), 13-25

CODEN: MDACAP; ISSN: 1699-3993

PB Prous Science

DT Journal; General Review

LA English

AB A review. Novel therapeutic strategies for type 2 diabetes are needed, since the current treatment options neither address all pathophysiol. mechanisms nor achieve the glycemic target goals. A general islet-cell dysfunction including insulin- and glucagon-secretion defects contributes to the pathophysiol. of type 2 diabetes. Improving islet function by incretin hormone action is a novel therapeutic approach. Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) are important incretin hormones contributing to 50-70% of the stimulation of insulin secretion after a meal. Dipeptidyl-peptidase IV (DPP-4) inhibitors inhibit the degradation of GLP-1 and GIP as well as that of other regulatory peptides. Sitagliptin, a DPP-4 inhibitor, is orally active and has been shown to be efficacious and safe in clin. studies. Sitagliptin has received approval in Mexico, the United States and other countries. Like other DPP-4 inhibitors, sitagliptin reduces Hb A1c (HbA1c), fasting and postprandial glucose by glucose-dependent stimulation of insulin secretion and inhibition of glucagon secretion. Sitagliptin is weight neutral. Indirect measures show a possible improvement of beta-cell function. Sitagliptin does not cause a higher rate of hypoglycemia in comparison to metformin or placebo. This article gives an overview of the mechanisms of action, pharmacol. and clin. trial results of sitagliptin.

IT 486460-32-6, Sitagliptin

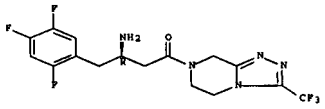
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sitagliptin was effective, safe and reduced Hb A1c, fasting and postprandial glucose by glucose-dependent stimulation of insulin secretion and inhibition of glucagon secretion in type 2 diabetes patient)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 19 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:412643 CAPLUS Full-text
DN 146:408429
TI Pharmaceutical formulations containing a dipeptidylpeptidase IV inhibitor
IN Joshi, Yatindra; Kowalski, James; Lakshman, Jay Parthiban; Royce, Alan Edward; Tong, Wei-Qin; Vasanthavada, Madhav
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 62pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

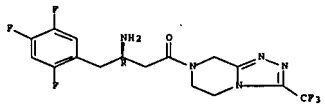
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007041053	A2	20070412	WO 2006-US37198	20060925
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-722624P	P	20050929		

AB This invention relates to a formulation comprising a dipeptidylpeptidase IV (DPP-IV) inhibitor preferably vildagliptin and metformin, to tablets comprising such formulations and to processes for the preparation thereof. Thus, tablet contained metformin HCl250.0, Klucel EXF 24.75, and Mg stearate 3.25 mg/tablet.
IT 654671-78-0, MK 0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical formulations containing dipeptidylpeptidase IV inhibitor)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 20 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:409270 CAPLUS Full-text
DN 146:415127
TI Dipeptidyl peptidase IV (DPP IV) inhibitor combination with immunosuppressive or immunomodulatory agent, and therapeutic use
IN Allison, Malcolm; Burkey, Bryan; Hughes, Thomas Edward; Kemp, Daniel Matthew
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 54pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

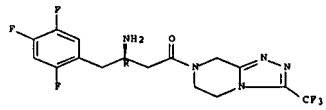
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007041368	A2	20070412	WO 2006-US38203	20060928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-722629P P 20050930

AB The invention discloses a combination, such as a combined preparation or pharmaceutical composition, resp., comprising of a DPP IV inhibitor, or a pharmaceutically acceptable salt thereof, and comprising at least one immunosuppressive or immunomodulator agent, or a pharmaceutically acceptable salt thereof. The invention furthermore discloses the use of such a combination for the prevention, delay of progression or treatment of diseases and disorders that may be inhibited by DPP IV inhibition, for the prevention, delay of progression or treatment of autoimmune diseases, and the disorders associated therewith, or for the prevention, delay of progression or treatment of graft rejection.
IT 486460-32-6, Sitagliptin 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibitor combination with immunosuppressive or immunomodulatory agent, and therapeutic use)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

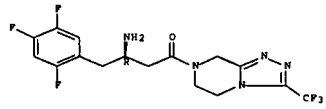


RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



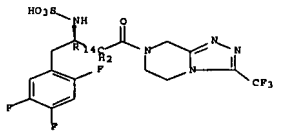
CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 21 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:407453 CAPLUS Full-text
DN 147:45133
TI Metabolism and excretion of the dipeptidyl peptidase 4 inhibitor [14C]sitagliptin in humans
AU Vincent, Stella H.; Reed, James R.; Bergman, Arthur J.; Elmore, Charles S.; Zhu, Bing; Xu, Shiyao; Ebel, David; Larson, Patrick; Zeng, Wei; Chen, Li; Dilzer, Stacy; Lasseter, Kenneth; Gottesdiener, Keith; Wagner, John A.; Herman, Gary A.
CS Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA
SO Drug Metabolism and Disposition (2007), 35(4), 533-538
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The metabolism and excretion of [14C]sitagliptin, an orally active, potent and selective dipeptidyl peptidase 4 inhibitor, were investigated in humans after a single oral dose of 83 mg/193 μCi. Urine, feces, and plasma were collected at regular intervals for up to 7 days. The primary route of excretion of radioactivity was via the kidneys, with a mean value of 87% of the administered dose recovered in urine. Mean fecal excretion was 13% of the administered dose. Parent drug was the major radioactive component in plasma, urine, and feces, with only 16% of the dose excreted as metabolites (13% in urine and 3% in feces), indicating that sitagliptin was eliminated primarily by renal excretion. Approx. 74% of plasma AUC of total radioactivity was accounted for by parent drug. Six metabolites were detected at trace levels, each representing <1 to 7% of the radioactivity in plasma. These metabolites were the N-sulfate and N-carbamoyl glucuronic acid conjugates of parent drug, a mixture of hydroxylated derivs., an ether glucuronide of a hydroxylated metabolite, and two metabolites formed by oxidative desatn. of the piperazine ring followed by cyclization. These metabolites were detected also in urine, at low levels. Metabolite profiles in feces were similar to those in urine and plasma, except that the glucuronides were not detected in feces. CYP3A4 was the major cytochrome P 450 isoenzyme responsible for the limited oxidative metabolism of sitagliptin, with some minor contribution from CYP2C8.
IT 939959-84-9 939959-86-1D, glucuronides 939959-87-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabolism and excretion of dipeptidyl peptidase 4 inhibitor [14C]sitagliptin in humans)
RN 939959-84-9 CAPLUS

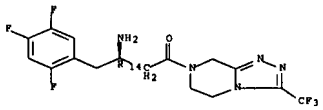
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



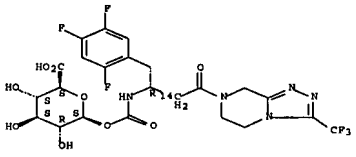
RN 939959-86-1 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 939959-87-2 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

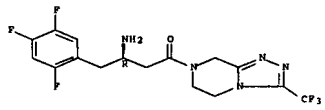
Absolute stereochemistry.



IT 486460-32-6, Sitagliptin 654671-78-0, Januvia
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metabolism and excretion of dipeptidyl peptidase 4 inhibitor [14C]sitagliptin in humans)
RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

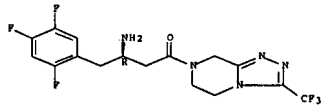


RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

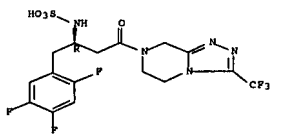
CRN 7664-38-2
CMF H3 O4 P

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:407452 CAPLUS Full-text

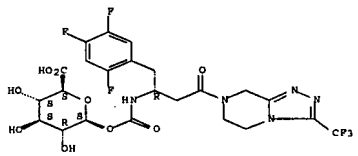
DN 147:45132
TI Disposition of the dipeptidyl peptidase 4 inhibitor sitagliptin in rats and dogs
AU Beconi, Maria G.; Reed, James R.; Teffera, Yohannes; Xia, Yuan-Qing; Kochansky, Christopher J.; Liu, David Q.; Xu, Shiyao; Elmore, Charles S.; Ciccotto, Suzanne; Hora, Donald F.; Stearns, Ralph A.; Vincent, Stella H.
CS Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA
SO Drug Metabolism and Disposition (2007), 35(4), 525-532
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The pharmacokinetics, metabolism, and excretion of sitagliptin [MK-0431; (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin- 7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine], a potent dipeptidyl peptidase 4 inhibitor, were evaluated in male Sprague-Dawley rats and beagle dogs. The plasma clearance and volume of distribution of sitagliptin were higher in rats (40-48 mL/min/kg, 7-9 l/kg) than in dogs (.apprx.9 mL/min/kg, .apprx.3 l/kg), and its half-life was shorter in rats, .apprx.2 h compared with .apprx.4 h in dogs. Sitagliptin was absorbed rapidly after oral administration of a solution of the phosphate salt. The absolute oral bioavailability was high, and the pharmacokinetics were fairly dose-proportional. After administration of [14C]sitagliptin, parent drug was the major radioactive component in rat and dog plasma, urine, bile, and feces. Sitagliptin was eliminated primarily by renal excretion of parent drug; biliary excretion was an important pathway in rats, whereas metabolism was minimal in both species in vitro and in vivo. Approx. 10 to 16% of the radiolabeled dose was recovered in the rat and dog excreta as phase I and II metabolites, which were formed by N-sulfation, N-carbamoyl glucuronidation, hydroxylation of the triazolopiperazine ring, and oxidative desatn. of the piperazine ring followed by cyclization via the primary amine. The renal clearance of unbound drug in rats, 32 to 39 mL/min/kg, far exceeded the glomerular filtration rate, indicative of active renal elimination of parent drug.
IT 940002-57-3 940002-59-5 940002-61-9
940002-62-0 940292-24-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(disposition of the dipeptidyl peptidase 4 inhibitor sitagliptin (MK-0431, Januvia) in rats and dogs)
RN 940002-57-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 940002-59-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

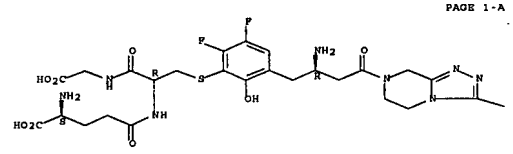
Absolute stereochemistry.



RN 940002-61-9 CAPLUS
CN Glycine, L-γ-glutamyl-S-[3-[(2R)-2-amino-4-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-oxobutyl]-5,6-difluoro-2-hydroxyphenyl]-L-cysteinyl- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

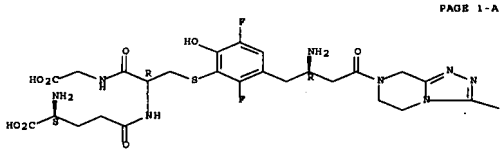


PAGE 1-B

RN 940002-62-0 CAPLUS
CN Glycine, L-γ-glutamyl-S-[3-[(2R)-2-amino-4-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-oxobutyl]-2,5-difluoro-6-hydroxyphenyl]-L-cysteinyl- (CA INDEX NAME)

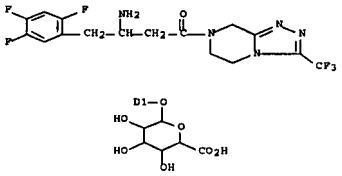
Absolute stereochemistry.

PAGE 1-A



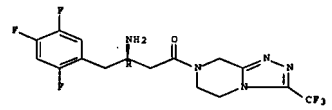
PAGE 1-B

RN 940292-24-0 CAPLUS
CN INDEX NAME NOT YET ASSIGNED



IT 486460-32-6, Sitagliptin
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(disposition of the dipeptidyl peptidase 4 inhibitor sitagliptin (MK-0431, Januvia) in rats and dogs)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

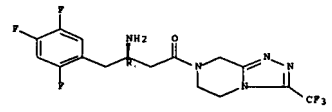
Absolute stereochemistry.



RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:407451 CAPLUS Full-text
DN 147:45131
TI Characterization of two cyclic metabolites of sitagliptin
AU Liu, David Q.; Arison, Byron H.; Stearns, Ralph A.; Kim, Dooseop; Vincent, Stella H.
CS Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA
SO Drug Metabolism and Disposition (2007), 35(4), 521-524
CODEN: DMDSAI; ISSN: 0090-9556
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Two novel metabolites of the dipeptidyl peptidase inhibitor sitagliptin (MK-0431, (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)-butan-2-amine), were identified after purification from dog urine. The metabolites (referred to as M2 and M5) were characterized by hydrogen/deuterium exchange tandem mass spectrometry and NMR spectroscopy nuclear Overhauser effect expts. as the cis and trans stereoisomers formed by cyclization of the primary amino group with the alpha carbon of the piperazine ring, following oxidative desatn.
IT 486460-32-6, Sitagliptin
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of two cyclic metabolites of sitagliptin)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

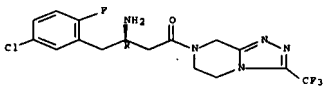
Absolute stereochemistry.



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

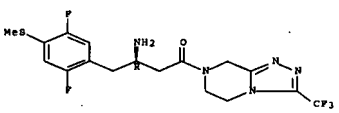
L11 ANSWER 24 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:403439 CAPLUS Full-text
DN 147:25788
TI Affinity-based ranking of ligands for DPP-4 from mixtures
AU Adam, Gregory C.; Meng, Juncai; Athanasopoulos, John; Zhang, Xiaoping; Chapman, Kevin T.
CS Department of Target Validation, Merck & Co., Inc., Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2007), 17(9), 2404-2407
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
AB Affinity-based selection strategies have recently emerged as a complement to traditional high throughput screening for the rapid discovery of lead compds. for the large number of protein targets emerging from omics technologies. Herein, we describe a method for the ranking of mixts. of ligands by affinity selection and apply it to rank order a set of inhibitors for the enzyme dipeptidyl peptidase IV.
IT 939402-83-2 939402-86-5 939402-90-1
939402-92-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(affinity-based ranking of ligands for DPP-4 from mixts.)
RN 939402-83-2 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



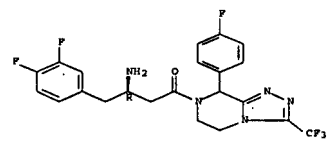
RN 939402-86-5 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



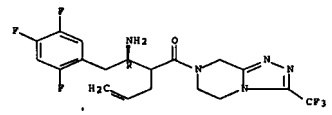
RN 939402-90-1 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RN 939402-92-3 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:383544 CAPLUS Full-text
DN 146:365787
TI Medical agent containing insulin resistance improving agent
IN Kanda, Shoichi; Nakashima, Ryutaro
PA Sankyo Company, Limited, Japan
SO PCT Int. Appl., 24pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2007037296	A1	20070405	WO 2006-JP319239	20060928

M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI JP 2005-283466 A 20050929

AB The present invention aims to provide a method for treating diabetes which exhibits excellent blood sugar lowering action, while having only few side effects. Specifically disclosed is a pharmaceutical product obtained by combining a DPP-IV inhibitor and an insulin resistance improving agent. For example, tablets were formulated containing rivoglitazone (as insulin resistance improving agent) and MK-0431 (DPP-IV inhibitor).

IT 654671-79-0, MK 0431 930279-24-6 930279-26-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceuticals containing DPP-IV inhibitor and insulin resistance improving agent.)

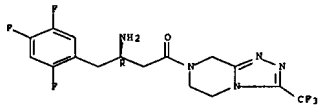
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

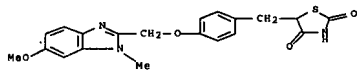
CRN 7664-38-2
CMF H3 O4 P

RN 930279-24-6 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(6-methoxy-1-methyl-1H-benzimidazol-2-yl)methoxy]phenyl]methyl]-, hydrochloride (1:1), mixt. with (3R)-3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-1-butanone phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 299176-11-7
CMF C20 H19 N3 O4 S . Cl H



● HCl

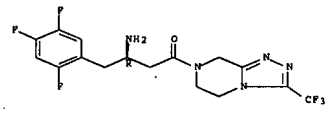
CM 2

CRN 654671-78-0
CMF C16 H15 F6 N5 O . H3 O4 P

CM 3

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 4

CRN 7664-38-2
CMF H3 O4 P

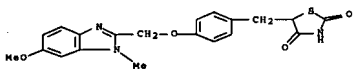
RN 930279-26-8 CAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[(6-methoxy-1-methyl-1H-benzimidazol-2-

yl)methoxy]phenyl]methyl]-, mixt. with (3R)-3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-1-butanone phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 185428-18-6
CMF C20 H19 N3 O4 S



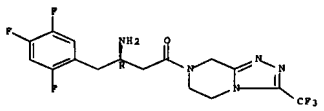
CM 2

CRN 654671-78-0
CMF C16 H15 F6 N5 O . H3 O4 P

CM 3

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 4

CRN 7664-38-2
CMF H3 O4 P

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 26 OF 100 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2007:360862 CAPLUS Full-text

DN 146:434793

TI Efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, compared with the sulfonylurea, glipizide, in patients with type 2 diabetes inadequately controlled on metformin alone: a randomized, double-blind, non-inferiority trial

AU Nauck, M. A.; Meininger, G.; Sheng, D.; Terranella, L.; Stein, P. P.

CS The Sitagliptin Study 024 Group, Diabeteszentrum Bad Lauterberg im Harz, Bad Lauterberg, Germany

SO Diabetes, Obesity and Metabolism (2007), 9(2), 194-205
CODEN: DOMEF6; ISSN: 1462-8902

PB Blackwell Publishing Ltd.

DT Journal

LA English

AB To compare the efficacy and safety of sitagliptin vs. glipizide in patients with type 2 diabetes and inadequate glycemic control [Hb A1c (HbA1c) ≥6.5 and ≤10%] on metformin monotherapy. After a metformin dose titration/stabilization period (≥1500 mg/day), 1172 patients were randomized to the addition of sitagliptin 100 mg q.d. (N = 588) or glipizide 5 mg/day (uptitrated to a potential maximum 20 mg/day) (N = 584) for 52 wk. The primary anal. assessed whether sitagliptin was non-inferior to glipizide regarding HbA1c changes from baseline at Week 52 using a per-protocol approach. From a mean baseline of 7.5%, HbA1c changes from baseline were -0.67% at Week 52 in both groups, confirming non-inferiority. The proportions achieving an HbA1c < 7% were 63% (sitagliptin) and 59% (glipizide). Fasting plasma glucose changes from baseline were -0.56 mmol/l (-10.0 mg/dL) and -0.42 mmol/l (-7.5 mg/dL) for sitagliptin and glipizide, resp. The proportion of patients experiencing hypoglycemia episodes was significantly ($p < 0.001$) higher with glipizide (32%) than with sitagliptin (5%), with 657 events in glipizide-treated patients compared with 50 events in sitagliptin-treated patients. Sitagliptin led to weight loss (change from baseline = -1.5 kg) compared with weight gain (+1.1 kg) with glipizide [between-treatment difference (95% confidence interval) = -2.5 kg (-3.1, -2.0); $p < 0.001$]. In this study, the addition of sitagliptin compared with glipizide provided similar HbA1c-lowering efficacy over 52 wk in patients on ongoing metformin therapy. Sitagliptin was generally well tolerated, with a lower risk of hypoglycemia relative to glipizide and with weight loss compared with weight gain with glipizide.

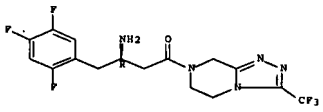
IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addition of sitagliptin compared with glipizide provided similar HbA1c-lowering efficacy in type 2 diabetes patient treated with metformin)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

RE.CNT 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD

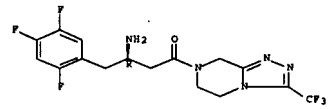


RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 27 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:360861 CAPLUS Full-text
DN 146:434792
TI Effect of adding sitagliptin, a dipeptidyl peptidase-4 inhibitor, to metformin on 24-h glycaemic control and β-cell function in patients with type 2 diabetes
AU Brazg, R.; Xu, L.; Man, C. Dalla; Cobelli, C.; Thomas, K.; Stein, P. P.
CS Rainier Clinical Research Center, Renton, WA, USA
SO Diabetes, Obesity and Metabolism (2007), 9(2), 186-193
CODEN: DOMEF6; ISSN: 1462-8902
PB Blackwell Publishing Ltd.
DT Journal
LA English
AB The aim of this study was to assess the effect of sitagliptin, a dipeptidyl peptidase-4 inhibitor, on 24-h glucose control when added to the regimen of patients with type 2 diabetes who had inadequate glycemic control on metformin therapy. In a double-blind, randomized, placebo-controlled, two-period crossover study, patients with type 2 diabetes with inadequate glycemic control on metformin monotherapy (i.e. on a stable dose of ≥1500 mg/day for ≥6 wk prior to the screening visit and an Hb A1c (HbA1c) ≥6.5% and <10% and fasting plasma glucose (FPG) ≤240 mg/dL) were recruited for participation. A total of 28 patients (baseline HbA1c range = 6.5-9.6%) receiving metformin were randomized into one of two treatment sequences: the addition of placebo for 4 wk followed by the addition of sitagliptin 50 mg twice daily (b.i.d.) for 4 wk, or vice versa. At the end of each treatment period, patients were domiciled for frequent blood sampling over 24 h. The primary endpoint was 24-h weighted mean glucose (WMG) and secondary endpoints included change in FPG, mean of 7 daily self-blood glucose measurements (MDG) and fructosamine. β-Cell function was assessed from glucose and C-peptide concns. were measured during the 5-h period after a standard breakfast meal by using the C-peptide minimal model. Despite a carryover effect from period 1 to period 2, the combined period 1 and period 2 results for glycemic endpoints were statistically significant for sitagliptin relative to placebo when added to ongoing metformin therapy. To account for the carryover effect, the period 1 results were also compared between the groups. Following period 1, there were significant least-squares (LS) mean redns. in 24-h WMG of 32.8 mg/dL, significant LS mean reduction from baseline in MDG of 28 mg/dL, FPG of 20.3 mg/dL and fructosamine of 33.7 mmol/l in patients treated with sitagliptin relative to placebo ($p < 0.05$). When added to ongoing metformin therapy, parameters of β-cell function were significantly improved with sitagliptin compared with placebo. No weight gain or increases in gastrointestinal adverse events or hypoglycemia events were observed with sitagliptin relative to placebo during this study. In this study, the addition of sitagliptin 50 mg b.i.d. to ongoing metformin therapy improved 24-h glycemic control and β-

cell function, and was generally well tolerated in patients with type 2 diabetes.
IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addition of sitagliptin to ongoing metformin therapy improved glycemic control and β-cell function and was generally well tolerated in type 2 diabetes patient)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

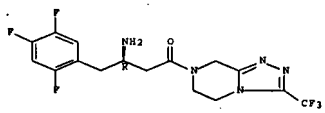


RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 28 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:360858 CAPLUS Full-text
DN 146:434012
TI Dipeptidyl peptidase-IV inhibitors: a major new class of oral antidiabetic drug
AU Idris, Iskandar; Donnelly, Richard
CS Department of Diabetes & Endocrinology, Sherwood Forest Hospitals NHS Trust, Mansfield, UK
SO Diabetes, Obesity and Metabolism (2007), 9(2), 153-165
CODEN: DOMEF6; ISSN: 1462-8902
PB Blackwell Publishing Ltd.
DT Journal; General Review
LA English
AB A review. Exploiting the incretin effect to develop new glucose-lowering treatments has become the focus of intense research. One successful approach has been the development of oral inhibitors of dipeptidyl peptidase-IV (DPP-IV). These drugs reversibly block DPP-IV-mediated inactivation of incretin hormones, for example, glucagon-like peptide 1 (GLP-1) and also other peptides that have alanine or proline as the penultimate N-terminal amino acid. DPP-IV inhibitors, therefore, increase circulating levels and prolong the biol. activity of endogenous GLP-1, but whether this is sufficient to fully explain the substantial reduction in Hb A1c (HbA1c) and associated metabolic profile remains open to further investigation. DPP-IV inhibitors such as vildagliptin and sitagliptin have been shown to be highly effective antihyperglycemic agents that augment insulin secretion and reduce glucagon secretion via glucose-dependent mechanisms. This review summarizes the major clin. trials with DPP-IV inhibitors as monotherapy and as add-on therapy in patients with type 2 diabetes. The magnitude of HbA1c reduction with DPP-IV inhibitors depends upon the pretreatment HbA1c values, but there seems to be no change in body weight, and very low rates of hypoglycemia and gastrointestinal disturbance with these agents. DPP-IV inhibitors represent a major new class

of oral antidiabetic drug and their metabolic profile offers a number of unique clin. advantages for the management of type 2 diabetes.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sitagliptin have been shown to be highly effective antihyperglycemic agents that augment insulin secretion and reduce glucagon secretion via glucose-dependent mechanisms in patient)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:351221 CAPLUS Full-text
DN 146:365734
TI Dodecylsulfate salt of a dipeptidyl peptidase-IV inhibitor
IN Ellison, Martha E.; Peresypkin, Andrey V.; Wenslow, Robert M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 25pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007035198	A2	20070329	WO 2006-US28504	20060721
WO 2007035198	A3	20070719		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

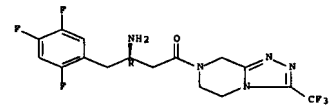
PRAI US 2005-702232P P 20050725
AB The dodecylsulfate salt of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo-[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine (I) is a potent inhibitor of dipeptidyl

peptidase-IV and is useful for the treatment of Type 2 diabetes. The invention also relates to a crystalline anhydrate of the dodecylsulfate salt as well as a process for its preparation, pharmaceutical compns. containing this novel form and methods of use for the treatment of type 2 diabetes, hyperglycemia, insulin resistance, and obesity. I was prepared in a series of steps. Th salt obtained was a crystalline anhydrous substance and characterized by x-ray powder diffraction.
IT 930277-01-3P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dodecylsulfate salt of a dipeptidyl peptidase-IV inhibitor)
RN 930277-01-3 CAPLUS
CN 1-Dodecanesulfonic acid, compd. with (3R)-3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-1-butanone (1:1) (CA INDEX NAME)

CM 1

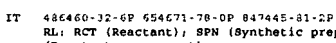
CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



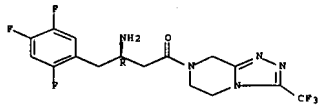
CM 2

CRN 1510-16-3
CMF C12 H26 O3 S



IT 486460-32-6P 654671-78-0P 847445-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(dodecylsulfate salt of a dipeptidyl peptidase-IV inhibitor)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

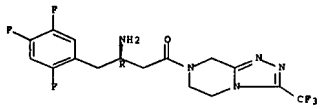


RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

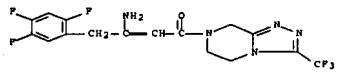
Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 847445-81-2 CAPLUS
CN 2-Buten-1-one, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)- (CA INDEX NAME)



L11 ANSWER 30 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:350563 CAPLUS Full-text
DN 146:330852
TI Use of a dipeptidyl peptidase IV (DPP-IV) inhibitor to reduce hypoglycemic events in antidiabetic treatment
IN Balkan, Boerk; Holmes, David Grenville; Hughes, Thomas Edward; Villhauer, Edwin Bernard
PA Novartis AG, Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 51pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

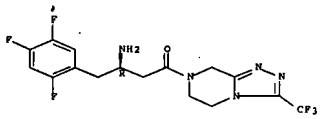
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007035665	A1	20070329	WO 2006-US36338	20060918

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-718856P P 20050920
US 2006-786755P P 20060328

AB The invention discloses a method to reduce the hypoglycemic events, especially severe hypoglycemic events resulting from insulin treatment, wherein the patient is treated with a dipeptidyl peptidase IV inhibitor (DPP-IV inhibitor), e.g. vildagliptin, or a pharmaceutically acceptable salt thereof.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibitors for reduction of hypoglycemic events in antidiabetic treatment)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

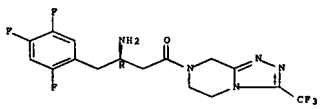
Absolute stereochemistry.



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 31 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:320887 CAPLUS Full-text
DN 146:394157
TI Dipeptidyl peptidase 4 inhibition with sitagliptin: a new therapy for Type 2 diabetes
AU Deacon, Carolyn F.
CS Panum Institute, Department of Biomedical Sciences, University of Copenhagen, Copenhagen N, DK-2200, Den.
SO Expert Opinion on Investigational Drugs (2007), 16(4), 533-545
CODEN: EOIDER; ISSN: 1354-3784
PB Informa Healthcare
DT Journal; General Review
LA English
AB A review. Sitagliptin is a once-daily, orally active, competitive and fully reversible inhibitor of dipeptidyl peptidase 4, the enzyme that is responsible for the rapid degradation of the incretin hormone glucagon-like peptide-1. It is the first in this new class of antihyperglycemic agents to gain regulatory approval for the treatment of Type 2 diabetes, both as a monotherapy and for use in combination with metformin or a thiazolidinedione. In clin. trials of ≤1-yr duration, sitagliptin improves glycemic control by reducing both fasting and postprandial glucose concns., leading to clin. meaningful redns. in glycosylated Hb levels. It is safe and well tolerated, with a side-effect profile that is similar to that of the placebo, a low incidence of hypoglycemia and body weight neutrality. Further clin. experience with sitagliptin will reveal its long-term durability, safety and efficacy.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase 4 inhibition with sitagliptin: a new therapy for Type 2 diabetes)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

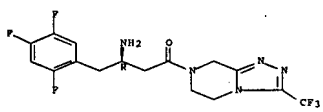
Absolute stereochemistry.



RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 32 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:299064 CAPLUS Full-text
DN 146:492585
TI Discovery and Structure-Activity Relationships of Piperidinone- and Piperidine-Constrained Phenethylamines as Novel, Potent, and Selective Dipeptidyl Peptidase IV Inhibitors
AU Pei, Zhonghua; Li, Xiaofeng; Von Geldern, Thomas W.; Longenecker, Kenton; Pireh, Daisy; Stewart, Kent D.; Backes, Bradley J.; Lai, Chunqiu; Lubben, Thomas H.; Ballaron, Stephen J.; Beno, David W. A.; Kempf-Grote, Anita J.; Sham, Hing L.; Trevillyan, James M.
CS Metabolic Disease Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA
SO Journal of Medicinal Chemistry (2007), 50(8), 1983-1987
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Dipeptidyl peptidase IV (DPP4) inhibitors are emerging as a new class of therapeutic agents for the treatment of type 2 diabetes. They exert their beneficial effects by increasing the levels of active glucagon-like peptide-1 and glucose-dependent insulinotropic peptide, which are two important incretins for glucose homeostasis. Starting from a high-throughput screening hit, we were able to identify a series of piperidinone- and piperidine-constrained phenethylamines as novel DPP4 inhibitors. Optimized compds. are potent, selective, and have good pharmacokinetic profiles.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Discovery and Structure-Activity Relationships of Piperidinone- and Piperidine-Constrained Phenethylamines as Novel, Potent, and Selective Dipeptidyl Peptidase IV Inhibitors)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

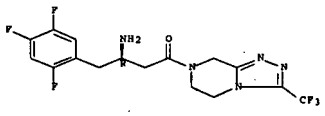


RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 33 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:237800 CAPLUS Full-text
DN 146:394936

TI Efficacy and tolerability of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy over 12 weeks in patients with type 2 diabetes
AU Scott, R.; Wu, M.; Sanchez, M.; Stein, P.
CS Christchurch School of Medicine, Christchurch, N. Z.
SO International Journal of Clinical Practice (2006), Volume Date 2007, 61(1), 171-180
CODEN: IJCPF9; ISSN: 1368-5031
PB Blackwell Publishing Ltd.
DT Journal
LA English
AB The aim of this study was to assess the efficacy and tolerability of the dipeptidyl peptidase-4 inhibitor, sitagliptin, in patients with type 2 diabetes who have inadequate glycemic control on diet and exercise. In a randomised, double-blind, placebo- and active-controlled study, 743 patients with type 2 diabetes and a mean baseline HbA1c of 7.9% were randomised to receive one of six treatments for 12 wk: placebo, sitagliptin 5, 12.5, 25 or 50 mg b.i.d., or glipizide 5 mg/day (electively titrated up to 20 mg/day). At week 12, treatment with sitagliptin at all doses tested led to a significant ($p < 0.001$) reduction in HbA1c relative to placebo, with the largest redns. occurring in the 50-mg b.i.d. group. The placebo-subtracted differences in HbA1c for the sitagliptin dose groups ranged from -0.38% to -0.77% in a dose-dependent manner, and -1.00% in the glipizide group. Sitagliptin also produced significant redns. in fasting plasma glucose and mean daily glucose across the dose range studied. Sitagliptin treatment was well tolerated and resulted in no significant weight change relative to placebo. There was a modest weight gain observed with glipizide treatment relative to placebo. Hypoglycemia adverse experiences were reported with the highest incidence in the glipizide group (17%) compared with the placebo (2%) or sitagliptin groups (0-4%, not dose-dependent). In summary, in this study sitagliptin improved glycemic control, with 50 mg b.i.d. being the most ED, and was generally well-tolerated in patients with type 2 diabetes.
IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and tolerability of sitagliptin in patients with type 2 diabetes)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 34 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:227665 CAPLUS Full-text
DN 146:244370

TI Drug containing FBPase inhibitor and DPP-IV inhibitor
IN Okuno, Akira; Yoshida, Taishi
PA Sankyo Company, Limited, Japan
SO PCT Int. Appl., 21pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007023754	A1	20070301	WO 2006-JP316292	20060821

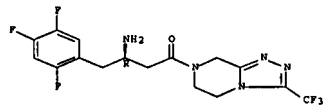
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI JP 2005-239310 A 20050822
OS MARPAT 146:244370
AB It is intended to provide a remedy for diabetes which exerts little side effects even in prolonged drug administration and is efficacious for a large number of diabetic patients. Disclosed is a drug comprising a combination of an fructose 1,6-biphosphatase (FBPase) inhibitor with a dipeptidyl peptidase IV (DPP-IV) inhibitor. Thus, the effect of combination of 2-amino-5-isobutyl-4-[2-[5-[N,N'-bis((S)-1- ethoxycarbonyl)ethyl]phosphonamide]furanyl]thiazole (I) and MK-0431 on glucose tolerance in Zucker Diabetic Fatty (ZDF) rats was examined Also, a capsule composition containing I 50, MK-0431 25, lactose 75, corn starch 50, and magnesium stearate 2 mg was formulated.
IT 654671-78-0, MK-0431 925668-18-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic drugs comprising combination of FBPase inhibitors and DPP-IV inhibitors)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

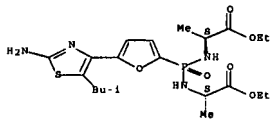
CRN 7664-38-2
CMF H3 O4 P

RN 925668-18-4 CAPLUS
CN L-Alanine, N,N'-[[5-[2-amino-5-(2-methylpropyl)-4-thiazolyl]-2-furanyl]phosphinylidene]bis-, 1,1'-diethyl ester, mixt. with (3R)-3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-1-butanone phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 280782-97-0
CMF C21 H33 N4 O6 P S

Absolute stereochemistry.



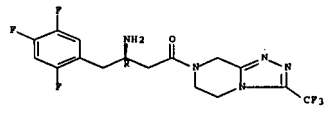
CM 2

CRN 654671-78-0
CMF C16 H15 F6 N5 O . H3 O4 P

CM 3

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 4

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 35 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:204629 CAPLUS Full-text
DN 146:329922
TI Effect of a single cyclosporine dose on the single-dose pharmacokinetics of sitagliptin (MK-0431), a dipeptidyl peptidase-4 inhibitor, in healthy male subjects
AU Krishna, Rajesh; Bergman, Arthur; Larson, Patrick; Cote, Josee; Lasseter, Kenneth; Dilzer, Stacey; Wang, Amy; Zeng, Wei; Chen, Li; Wagner, John; Herman, Gary
CS Merck and Co, Inc, Whitehouse Station, NJ, USA
SO Journal of Clinical Pharmacology (2007), 47(2), 165-174
CODEN: JCPCBR; ISSN: 0091-2700
PB Sage Publications
DT Journal
LA English
AB Sitagliptin (MK-0431) is an orally active, potent, and selective dipeptidyl peptidase-4 inhibitor used for the treatment of patients with type 2 diabetes mellitus. Sitagliptin has been shown to be a substrate for P-glycoprotein in preclin. studies. Cyclosporine was used as a probe P-glycoprotein inhibitor at a high dose to evaluate the potential effect of potent P-glycoprotein inhibition on single-dose sitagliptin pharmacokinetics in healthy male subjects. Eight healthy young men received a single oral 600-mg dose of cyclosporine with a single 100-mg oral sitagliptin dose and a single oral 100-mg sitagliptin dose alone in an open-label, randomized, 2-period, crossover study. Single doses of sitagliptin with or without single doses of cyclosporine were generally well tolerated. The sitagliptin AUC0-∞ geometric mean ratio was 1.29 with a 90% confidence interval of (1.24, 1.34). The sitagliptin Cmax geometric mean ratio was 1.68 with a 90% confidence interval of (1.35, 2.08). Cyclosporine coadministration did not appear to affect apparent sitagliptin renal clearance, t1/2, or C24 h, suggesting that effects

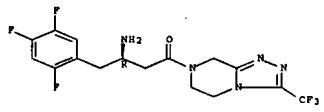
of these high doses of cyclosporine are more likely due to enhanced absorption of sitagliptin, potentially through inhibition of intestinal P-glycoprotein. These results rationalize the use of a single high-dose cyclosporine as a probe inhibitor of P-glycoprotein for compound candidates whose elimination is less dependent on CYP3A4-mediated metabolism

IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single dose of sitagliptin with or without Neoral was well tolerated and latter did not appear to affect renal clearance but modestly increased maximal plasma concentration of former in healthy male subject)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 36 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:204628 CAPLUS Full-text
DN 146:329921
TI Multiple-dose administration of sitagliptin, a dipeptidyl peptidase-4 inhibitor, does not alter the single-dose pharmacokinetics of rosiglitazone in healthy subjects
AU Mistry, Goutam C.; Bergman, Arthur J.; Luo, Wen-Lin; Cilissen, Caroline; Haazen, Wouter; Davies, Michael J.; Gottesdiener, Keith M.; Wagner, John A.; Herman, Gary A.
CS Merck and Co, Inc, Whitehouse Station, NJ, USA
SO Journal of Clinical Pharmacology (2007), 47(2), 159-164
CODEN: JCPCBR; ISSN: 0091-2700
PB Sage Publications
DT Journal
LA English
AB Sitagliptin, a dipeptidyl peptidase-4 inhibitor, is an incretin enhancer that is approved for the treatment of type 2 diabetes. Sitagliptin is mainly renally eliminated and not a potent inhibitor of CYP450 enzymes in vitro. Rosiglitazone, a thiazolidenedione, is an insulin sensitizer and mainly metabolized by CYP2C8. Since both agents may potentially be coadministered, the purpose of this study was to examine the effects of sitagliptin on rosiglitazone pharmacokinetics. In this open-label, randomized, 2-period, crossover study, 12 healthy normoglycemic subjects, 21 to 44 years, received single 4-mg doses of rosiglitazone alone in one period and coadministered with sitagliptin on day 5 following a multiple-dose regimen for sitagliptin (200 mg once daily + 5 days) in the other period. The geometric mean ratios and 90% confidence intervals ([rosiglitazone + sitagliptin]/rosiglitazone) for rosiglitazone AUC0-∞ and Cmax were 0.98 (0.93, 1.02) and 0.99 (0.88, 1.12),

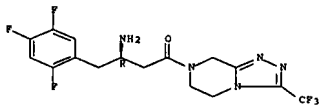
resp. In conclusion, sitagliptin did not alter the pharmacokinetics of rosiglitazone in healthy subjects.

IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration of multiple-dose sitagliptin did not alter single-dose pharmacokinetics of Avandia in healthy human)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 37 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:173034 CAPLUS Full-text
DN 146:236092
TI Composition comprising DPP-IV inhibitor
IN Loeffler, Bernd Michael; MacDonald, Alexander; Rocha, Cynthia; Worth, Eric
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 58pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007017423	A2	20070215	WO 2006-EP64933	20060802
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2007098781	A1	20070503	US 2006-499587	20060804
PRAI EP 2005-107393	A	20050811		

OS MARPAT 146:236092
AB The present invention refers to pharmaceutical composition comprising a DPP-IV inhibitor. Thus, coated tablet 100 mg was prepared comprising (2S)-1-{[1,1-dimethyl-3-(4-pyridin-3-yl-imidazol-1-yl)-propylamino]- acetyl}-pyrrolidine-2-

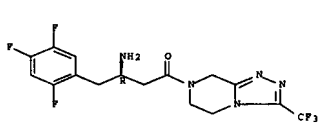
carbonitrile 50 mg, Avicel PH-101 56.4 mg, sodium stearyl fumarate 4.8125 mg, talc 1.925 mg, and Eudragit S: Eudragit L (25:75) 25 mg.

IT 486460-32-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising DPP-IV inhibitor)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 38 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:61707 CAPLUS Full-text
DN 146:149027
TI Composition comprising combination of cannabinoid receptor-1 antagonist and DPP-IV inhibitor
IN Milosavljevic-Ristic, Smiljana
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 49pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2007006790	A2	20070118	WO 2006-EP64117	20060711
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-698304P	P	20050712		

AB The present invention relates to a combination, such as a combined preparation or pharmaceutical composition, resp., comprising of a DPP IV inhibitor or a pharmaceutically acceptable salt thereof and comprising at least one CB1 antagonist, or a pharmaceutically acceptable salt thereof. The present invention furthermore relates to the use of such a combination for the prevention of, delay of progression of, treatment of diseases and disorders that may be inhibited by DPP IV inhibition, appetency disorders or substance

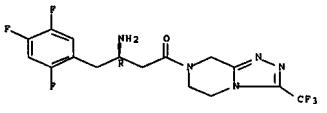
abuse disorders. Thus, combination of vildagliptin 50 mg and rimionabant 20 mg was used for improvement of cognitive function.

IT 486460-32-6, Sitagliptin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising combination of cannabinoid receptor-1 antagonist and DPP-IV inhibitor)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



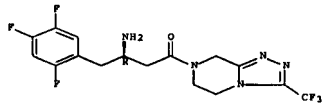
L11 ANSWER 39 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:10527 CAPLUS Full-text
DN 146:135224
TI Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin added to ongoing metformin therapy in patients with type 2 diabetes inadequately controlled with metformin alone
AU Charbonnel, Bernard; Karasik, Avraham; Liu, Ji; Wu, Mei; Meininger, Gary
CS SITAGLIPTIN STUDY 020 GROUP, Centre Hospitalier Universitaire de Nantes, Nantes, Fr.
SO Diabetes Care (2006), 29(12), 2638-2643
CODEN: DICAD2; ISSN: 0149-5992
PB American Diabetes Association, Inc.
DT Journal
LA English
AB The efficacy and safety of the dipeptidyl peptidase-4 inhibitor, sitagliptin, added to ongoing metformin therapy, were assessed in patients with type 2 diabetes who had inadequate glycemic control (HbA1c [A1C] ≥7 and ≤10%) with metformin alone. After a screening diet/exercise run-in period, a metformin dose titration/stabilization period, and a 2-wk, single-blind, placebo run-in period, 701 patients, aged 19-78 years, with mild to moderate hyperglycemia (mean A1C 8.0%) receiving ongoing metformin (≥1,500 mg/day) were randomly assigned to receive the addition of placebo or sitagliptin 100 mg once-daily in a 1:2 ratio for 24 wk. Patients exceeding specific glycemic limits were provided rescue therapy (pioglitazone) until the end of the study. The efficacy analyses were based on an all-patients-treated population using an ANCOVA and excluded data obtained after glycemic rescue. At week 24, sitagliptin treatment led to significant redns. compared with placebo in A1C (-0.65%), fasting plasma glucose, and 2-h postmeal glucose. Fasting insulin, fasting C-peptide, fasting proinsulin-to-insulin ratio, postmeal insulin and C-peptide areas under the curve (AUCs), postmeal insulin AUC-to-glucose AUC ratio, homeostasis model assessment of β-cell function, and quant. insulin sensitivity check index were significantly improved with sitagliptin relative to placebo. A significantly greater proportion of patients achieved an A1C <7% with sitagliptin (47.0%) than with placebo (18.3%). There was no

increased risk of hypoglycemia or gastrointestinal adverse experiences with sitagliptin compared with placebo. Body weight decreased similarly with sitagliptin and placebo. Sitagliptin 100 mg once-daily added to ongoing metformin therapy was efficacious and well tolerated in patients with type 2 diabetes who had inadequate glycemic control with metformin alone.

IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sitagliptin 100 mg once-daily added to ongoing metformin therapy was efficacious and well tolerated in patient with type 2 diabetes who had inadequate glycemic control with metformin alone)

RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

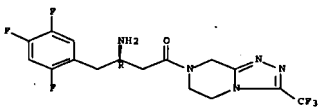
L11 ANSWER 40 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:10526 CAPLUS Full-text
DN 146:135223
TI Effect of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy on glycemic control in patients with type 2 diabetes
AU Aschner, Pablo; Kipnes, Mark S.; Lunceford, Jared K.; Sanchez, Matilde; Mickel, Carolyn; Williams-Herman, Debora E.
CS SITAGLIPTIN STUDY 021 GROUP, Colombian Diabetes Association, Bogota, Colombia
SO Diabetes Care (2006), 29(12), 2632-2637
CODEN: DICAD2; ISSN: 0149-5992
PB American Diabetes Association, Inc.
DT Journal
LA English
AB To examine the efficacy and safety of once-daily oral sitagliptin as monotherapy in patients with type 2 diabetes. In a randomized, double-blind, placebo-controlled study, 741 patients (baseline HbA1c [A1C] 8.0%) were randomized to sitagliptin 100 or 200 mg or placebo for 24 wk. Sitagliptin 100 and 200 mg produced significant ($P < 0.001$) placebo-subtracted redns. in A1C (-0.79 and -0.94%, resp.) and fasting plasma glucose (-1.0 mmol/l [-17.1 mg/dL] and -1.2 mmol/l [-21.3 mg/dL], resp.). Patients with baseline A1C ≥9% had greater redns. in placebo-subtracted A1C with sitagliptin 100 and 200 mg (-1.52 and -1.50%, resp.) than those with baseline A1C <8% (-0.57 and -0.65%) or ≥8 to <9.0% (-0.80 and -1.13%, resp.). In a meal tolerance test, sitagliptin 100 and 200 mg significantly decreased 2-h postprandial glucose (PPG) (placebo-subtracted PPG -2.6 mmol/l [-46.7 mg/dL] and -3.0 mmol/l [-54.1 mg/dL], resp.). Results for the above key efficacy parameters were not significantly different between sitagliptin doses. Homeostasis model

assessment of β-cell function and proinsulin-to-insulin ratio improved with sitagliptin. The incidence of hypoglycemia was similar, and overall gastrointestinal adverse experiences were slightly higher with sitagliptin. No meaningful body weight changes from baseline were observed with sitagliptin 100 (-0.2 kg) or 200 mg (-0.1 kg). The body weight change with placebo (-1.1 kg) was significantly ($P < 0.01$) different from that observed with sitagliptin. In this 24-wk study, once-daily sitagliptin monotherapy improved glycemic control in the fasting and postprandial states, improved measures of β-cell function, and was well tolerated in patients with type 2 diabetes.

IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(once daily sitagliptin monotherapy improved glycemic control in patient with type 2 diabetes)

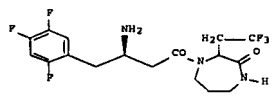
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 41 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2007:2727 CAPLUS Full-text
DN 146:176193
TI (3R)-4-[(3R)-3-Amino-4-(2,4,5-trifluorophenyl)butanoyl]-3-(2,2,2-trifluoroethyl)-1,4-diazepan-2-one, a selective dipeptidyl peptidase IV inhibitor for the treatment of type 2 diabetes
AU Biftu, Tesfaye; Feng, Dennis; Qian, Xiaoxia; Liang, Gui-Bai; Kieczykowski, Gerard; Eiermann, George; He, Huaibing; Leiting, Barbara; Lyons, Kathy; Petrov, Aleksandr; Sinha-Roy, Ranabir; Zhang, Bei; Scapin, Giovanna; Patel, Sangita; Gao, Ying-Duo; Singh, Suresh; Wu, Joseph; Zhang, Xiaoping; Thornberry, Nancy A.; Weber, Ann E.
CS Department of Medicinal Chemistry, Merck Research Laboratories, Merck & Co., Inc., Rahway, NJ, 07065, USA
SO Bioorganic & Medicinal Chemistry Letters (2007), 17(1), 49-52
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Ltd.
DT Journal
LA English
GI



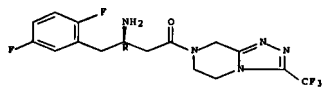
I

AB Replacement of the triazolopiperazine ring of sitagliptin (DPP-4 IC50 = 18 nM) with 3-(2,2,2-trifluoroethyl)-1,4-diazepan-2-one gave dipeptidyl peptidase IV (DPP-4) inhibitor I which is potent (DPP-4 IC50 = 2.6 nM), selective, and efficacious in an oral glucose tolerance test in mice. It was selected for extensive preclin. development as a potential back-up candidate to sitagliptin.

IT 486460-31-5 486460-32-6, Sitagliptin 611240-24-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diazepanones as dipeptidyl peptidase IV inhibitors)

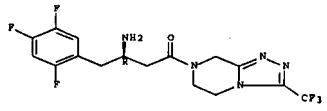
RN 486460-31-5 CAPLUS
CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



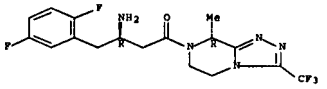
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 611240-24-5 CAPLUS
CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[(8R)-5,6-dihydro-8-methyl-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

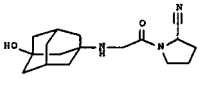


RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 42 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1338372 CAPLUS Full-text
DN 146:68738
TI Direct compression formulation of dipeptidylpeptidase IV inhibitors
IN Kowalski, James; Lakshman, Jay Parthiban; Patel, Arun P.
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 59pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006135693	A2	20061221	WO 2006-US22336	20060608
	WO 2006135693	A3	20070215		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI	US 2005-689739P	P	20050610		
	US 2005-690527P	P	20050614		
	US 2005-690814P	P	20050615		

GI



I

AB Dipeptidylpeptidase IV inhibitor (herein referred to as DPP-IV) that may be 98.5 100% pure is a high-dose drug capable of being directly compressed with a glitazone and specific excipients into sold form dosage forms, such as tablets and capsules having desired, hardness, disintegrating ability and acceptable dissoln. characteristics. DPP-IV is not inherently compressible and thus presents formulation problems. Excipients used in the formulation enhance the flow and compaction properties of the drug and tableting mix. Optimal flow contributes to uniform die fill and weight control. The binder used ensures sufficient cohesive properties that allow DPP-IV to be compressed using the direct compression method. The tablets produced provide an acceptable in vitro dissoln. profile. Tablets were prepared containing vildagliptin (I) (DPP-IV inhibitor), pioglitazone, microcryst. cellulose, Na starch glycolate and Mg stearate.

IT 654671-70-0, MK-0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(direct compression formulation of dipeptidylpeptidase IV inhibitors)

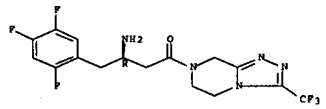
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.

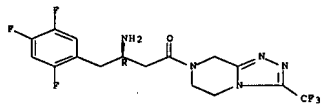


CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 43 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1328538 CAPLUS Full-text
DN 146:433889
TI DPPIV inhibitor
AU Igarashi, Yasuhiro; Watada, Hirotaka; Kawamori, Ryuzo
CS Department of Medicine, Metabolism and Endocrinology, Juntendo University School of Medicine, Tokyo, 113-8421, Japan
SO Naibunpi, Tonyobyoka (2006), 23(3), 291-298
CODEN: NATOFF; ISSN: 1341-3724
PB Kagaku Hyoronsha
DT Journal; General Review
LA Japanese
AB A review, discussing the action mechanism, toxicity, and clin. pharmacol. of DPPIV (dipeptidyl peptidase-IV) inhibitors, including vildagliptin and sitagliptin, as oral antidiabetics for treatment of type 2 diabetes.
IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(action mechanism, toxicity, and clin. pharmacol. of DPPIV (dipeptidyl peptidase-IV) inhibitors, including vildagliptin and sitagliptin, as oral antidiabetics for treatment of type 2 diabetes)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 44 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1326428 CAPLUS Full-text
DN 146:114748
TI Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin added to ongoing pioglitazone therapy in patients with type 2 diabetes: a 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group study
AU Rosenstock, Julio; Brazg, Ronald; Andryuk, Paula J.; Lu, Kaifeng; Stein, Peter
CS Sitagliptin Study 019 Group, Dallas Diabetes and Endocrine Center, Dallas, TX, USA
SO Clinical Therapeutics (2006), 28(10), 1556-1568
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English
AB Objective: The efficacy and tolerability of the dipeptidyl peptidase-4 inhibitor sitagliptin added to ongoing pioglitazone therapy were assessed in patients with type 2 diabetes and inadequate glycemic control (glycosylated Hb [HbA1c] ≥7% and ≤10%) while receiving a stable dose of pioglitazone. Methods:

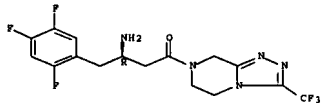
This was a 24-wk, multicenter, randomized, double-blind, placebo-controlled, parallel-group study in patients aged ≥18 years (ClinicalTrials. gov NCT00086502). At screening, all patients began a diet/exercise program that continued throughout the study period. Patients taking antihyperglycemic therapy other than pioglitazone underwent a washout of this therapy and entered an 8- to 14-wk open-label pioglitazone dose-titration/stabilization period. Patients with an HbA1c ≥7% and ≤10% at the end of this period entered a 2-wk, single-blind, placebo run-in period (total duration of run-in period, up to 21 wk). Patients who had been receiving pioglitazone monotherapy (30 or 45 mg/d) and had an HbA1c ≥7% and ≤10% entered the 2-wk, single-blind, placebo run-in period directly. Thus, at the time of randomization, all patients were receiving ongoing pioglitazone (30 or 45 mg/d). Patients were randomized in a 1:1 ratio to receive sitagliptin 100 mg once daily or placebo for 24 wk. The primary efficacy end point was the change from baseline in HbA1c at week 24. Secondary efficacy end points included the change from baseline in fasting plasma glucose (FPG), insulin, and proinsulin; the Homeostasis Model Assessment β-cell function and insulin-resistance indexes; the proinsulin/insulin ratio; the Quant. Insulin Sensitivity Check Index; the percent changes from baseline in selected lipid parameters; the proportion of patients meeting the American Diabetes Association HbA1c goal of <7.0%; the proportion of patients requiring metformin rescue therapy; and the time to the initiation of rescue therapy. Results: One hundred seventy-five patients were randomized to receive sitagliptin, and 178 were randomized to receive placebo. The mean (SD) baseline HbA1c value was 8.1% (0.8) in the sitagliptin group and 8.0% (0.8) in the placebo group. After 24 wk, sitagliptin added to pioglitazone therapy was associated with significant redns. compared with placebo in HbA1c (between-treatment difference in least squares [LS] mean change from baseline: -0.70%; 95% CI, -0.85 to -0.54; P < 0.001) and FPG (-17.7 mg/dL; 95% CI, -24.3 to -11.0; P < 0.001). Mean HbA1c values at end point were 7.2% (0.9) and 7.8% (1.1) in the resp. treatment groups, and the proportions of patients reaching a target HbA1c of <7.0% were 45.4% and 23.0% (P < 0.001). Significant redns. in fasting serum proinsulin levels and the proinsulin/insulin ratio were seen with sitagliptin treatment compared with placebo (both, P < 0.01). Sitagliptin was generally well tolerated, with no increased risk of hypoglycemia compared with placebo (2 vs 0 patients, resp.). The number of patients discontinuing the study due to clin. adverse experiences (10 [5.7%] vs 2 [1.1%]) and the incidence of abdominal pain (3.4% vs 0%) were significantly greater in the sitagliptin group compared with the placebo group (both, P < 0.05). The LS mean change in body weight from baseline did not differ significantly between sitagliptin or placebo added to pioglitazone therapy (between-treatment difference in LS mean change from baseline: 0.2 kg; 95% CI, -0.5 to 1.0). Conclusion: In this 24-wk study, sitagliptin 100 mg once daily added to ongoing pioglitazone therapy was effective and well tolerated in these patients with type 2 diabetes who had not achieved adequate glycemic control with pioglitazone alone.

IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase-4 inhibitor sitagliptin added to pioglitazone therapy reduced glycosylated Hb, fasting plasma glucose and proinsulin than pioglitazone alone in patient with type 2 diabetes mellitus)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 45 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1320516 CAPLUS Full-text
DN 146:114024
TI DPP-4 inhibitors and their potential role in the management of type 2 diabetes
AU Barnett, A.
CS Department of Medicine, University of Birmingham and Heart of England National Health Service Foundation Trust(Teaching), Birmingham, UK
SO International Journal of Clinical Practice (2006), 60(11), 1454-1470
CODEN: IJCPF9; ISSN: 1368-5031
PB Blackwell Publishing Ltd.
DT Journal; General Review
LA English
AB A review. The dipeptidyl peptidase 4 (DPP-4) inhibitors enhance the body's own ability to control blood glucose by increasing the active levels of incretin hormones in the body. Their mechanism of action is distinct from any existing class of oral glucose-lowering agents. They control elevated blood glucose by triggering pancreatic insulin secretion, suppressing pancreatic glucagon secretion, and signalling the liver to reduce glucose production The leading DPP-4 inhibitors have shown clin. significant HbA1c redns. up to 1 yr of treatment and offer many potential advantages over existing diabetes therapies including a low risk of hypoglycemia, no effect on body weight, and the potential, based on animal and in vitro studies, for the regeneration and differentiation of pancreatic β-cells. They are efficacious as monotherapy and also in combination with commonly prescribed antidiabetic agents and are suitable for once-daily oral dosing. Consequently, many DPP-4 inhibitors such as vildagliptin (Galvus; LAF-237), sitagliptin (Januvia; MK-0431), and saxagliptin (BMS-477118) have advanced into late-stage human clin. trials. Search strategy and selection criteria This review was built on a systematic MEDLINE search for publications on the subject with the key words: DPP-4 inhibitor; vildagliptin (LAF-237); sitagliptin (MK-0431); saxagliptin (BMS-477118); and type 2 diabetes; up to August 2006. Meeting abstrs. were also searched, as much of the data currently only exists in abstract form. Take home message for clinician The DPP-4 inhibitors appear to have great potential for the treatment of type 2 diabetes, but time will tell if this will be realized. While they do not lower glucose to a greater extent than existing therapies, they offer many potential advantages, including the ability to achieve sustainable redns. in HbA1c with a well-tolerated agent that has a low risk of hypoglycemia and no weight gain, and which can be administered as a once-daily oral dose.

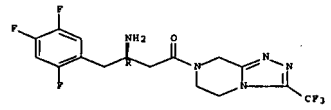
IT 654671-78-0, Januvia
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase 4 inhibitor Januvia might have role in management of type 2 diabetes in human)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

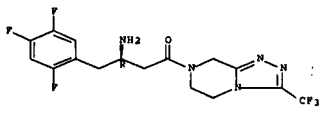
CRN 7664-38-2
CMF H3 O4 P

RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 46 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1274234 CAPLUS Full-text
DN 146:49995
TI The development of a stable, coated pellet formulation of a water-sensitive drug, a case study: development of a stable core formulation
AU Fitzpatrick, Shaun; Taylor, Scott; Booth, Steven W.; Newton, Michael J.
CS Development Laboratories, Merck Sharp and Dohme Ltd., Hoddesdon, Herts, UK
SO Pharmaceutical Development and Technology ((2006)), 11(4), 521-528
CODEN: PDTEFS; ISSN: 1083-7450
PB Taylor & Francis, Inc.
DT Journal
LA English
AB A development program has been carried out to provide a stable extrusion/spheronization pellet formulation for a highly water-soluble drug, sitagliptin, which undergoes a change in phys. form on processing and is subject to hydrolytic decomposition A conventional extrusion/spheronization formulation resulted in significant degradation of the drug. The inclusion of

glyceryl monostearate into the formulation was found to reduce the water levels required to such a level that there was no significant degradation of the drug during processing to form pellets. The use of a ram extruder to screen formulations with small quantities minimizes the need for the drug in the formulation-screening process, and the results from this method of extrusion were found to be translatable to the use of a screen extruder, which allowed scale-up of the process.
IT 486460-32-6, Sitagliptin
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(stable, coated pellet formulation of a water-sensitive drug with a stable core formulation)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

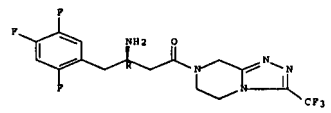


RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 47 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1266432 CAPLUS Full-text
DN 146:92587
TI Tolerability and pharmacokinetics of metformin and the dipeptidyl peptidase-4 inhibitor sitagliptin when co-administered in patients with type 2 diabetes
AU Herman, Gary A.; Bergman, Arthur; Yi, Bingming; Kipnes, Mark
CS Sitagliptin Study 012 Group, Merck Research Laboratories, Rahway, NJ, USA
SO Current Medical Research and Opinion ((2006)), 22(10), 1939-1947
CODEN: CMROCX; ISSN: 0300-7995
PB LibraPharm Ltd.
DT Journal
LA English
AB Objective: As part of the clin. development of sitagliptin, a dipeptidyl peptidase-4 inhibitor, for the treatment of type 2 diabetes, the potential for pharmacokinetic interactions with other antihyperglycemic agents used in managing patients with type 2 diabetes are being carefully evaluated. The purposes of this study were to evaluate the tolerability of co-administered sitagliptin and metformin and effects of sitagliptin on metformin pharmacokinetics as well as metformin on sitagliptin pharmacokinetics under steady-state conditions. Methods: This placebo-controlled, multiple-dose, crossover study in patients with type 2 diabetes assessed the tolerability of co-administered sitagliptin (50 mg b.i.d.) with metformin (1000 mg b.i.d.). Patients received, in a randomized crossover manner, three treatments (each of 7 days duration): 50 mg sitagliptin twice daily and placebo to metformin twice daily; 1000 mg of metformin twice daily and placebo to sitagliptin twice daily; concomitant administration of 50 mg of sitagliptin twice daily and 1000

mg of metformin twice daily. Following dosing on Day 7 of each treatment period, these pharmacokinetic parameters were determined for plasma sitagliptin and metformin: area under the plasma concns.-time curve over the dosing interval (AUC0-12 h), maximum observed plasma concns. (Cmax), and time of occurrence of maximum observed plasma concns. (Tmax). Renal clearance was also determined for sitagliptin. Results: In this study, no adverse experiences were reported by 11 of 13 patients. Two patients had adverse experiences, which were not related to study drugs as determined by the investigators. The mean metformin plasma concentration-time profiles were nearly identical with or without sitagliptin co-administration [metformin AUC0-12 h geometric mean ratio (GMR; [metformin + sitagliptin]/metformin)] was 1.02 (90% CI 0.95, 1.09). Similarly metformin administration did not alter the plasma sitagliptin pharmacokinetics [sitagliptin AUC0-12 h GMR ([sitagliptin + metformin]/sitagliptin)] was 1.02 (90% CI 0.97, 1.08) or renal clearance of sitagliptin. No efficacy measurements (glycosylated Hb or fasting plasma glucose) were obtained during this study. Urinary pharmacokinetics for metformin were not determined due to the lack of effect of sitagliptin on plasma metformin pharmacokinetics. Conclusions: In this study, co-administration of sitagliptin and metformin was generally well tolerated in patients with type 2 diabetes and did not meaningfully alter the steady-state pharmacokinetics of either agent.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration of sitagliptin and metformin was well tolerated and did not alter steady-state pharmacokinetics of either agent in patient with type 2 diabetes)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



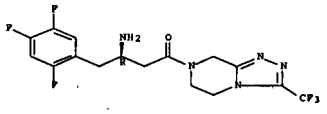
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 48 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1256551 CAPLUS Full-text
DN 146:20305
TI Combination of a dipeptidyl peptidase-IV inhibitor and a dual PPAR agonist for the treatment of diabetes and obesity
IN Thornberry, Nancy A.; Kaufman, Keith D.
PA USA
SO U.S. Pat. Appl. Publ., 23pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2006270722	A1	20061130	US 2006-440198	20060524
PRAI	US 2005-686076P	P	20050531		

AB The present invention relates to pharmaceutical compns. comprising a combination of a particular dipeptidyl peptidase-IV (DPP-IV) inhibitor and a particular PPAR-α/γ dual agonist, kits containing such combinations and methods of using such compns. for the treatment of diabetes, diabetes associated with obesity, diabetes-related disorders, obesity, and obesity-related disorders.
IT 486460-32-6P 654671-78-0P, MK-0431
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(combination of dipeptidyl peptidase-IV inhibitor and dual PPAR agonist for treatment of diabetes and obesity)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

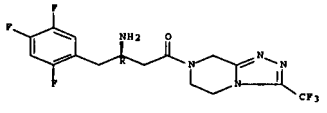


RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

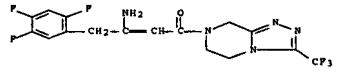
Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

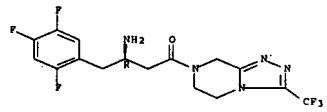
IT 847445-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(combination of dipeptidyl peptidase-IV inhibitor and dual PPAR agonist for treatment of diabetes and obesity)
RN 847445-81-2 CAPLUS
CN 2-Buten-1-one, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)- (CA INDEX NAME)



L11 ANSWER 49 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1212876 CAPLUS Full-text
DN 146:38812
TI Effect of single oral doses of sitagliptin, a dipeptidyl peptidase-4 inhibitor, on incretin and plasma glucose levels after an oral glucose tolerance test in patients with type 2 diabetes
AU Herman, Gary A.; Bergman, Arthur; Stevens, Catherine; Kotey, Paul; Yi, Bingming; Zhao, Peng; Dietrich, Bruno; Golor, George; Schrodter, Andreas; Keymeulen, Bart; Lasseter, Kenneth C.; Kipnes, Mark S.; Snyder, Karen; Hilliard, Deborah; Tanen, Michael; Cilissen, Caroline; De Smet, Marina; de Lepeleire, Inge; Van Dyck, Kristien; Wang, Amy Q.; Zeng, Wei; Davies, Michael J.; Tanaka, Wesley; Holst, Jens J.; Deacon, Carolyn F.; Gottesdiener, Keith M.; Wagner, John A.
CS Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Journal of Clinical Endocrinology and Metabolism (2006), 91(11), 4612-4619
CODEN: JCEMAZ; ISSN: 0021-972X
PB Endocrine Society
DT Journal
LA English
AB In response to a meal, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) are released and modulate glycemic control. Normally these incretins are rapidly degraded by dipeptidyl peptidase-4 (DPP-4). DPP-4 inhibitors are a novel class of oral antihyperglycemic agents in development for the treatment of type 2 diabetes. The degree of DPP-4 inhibition and the level of active incretin augmentation required for glucose lowering efficacy after an oral glucose tolerance test (OGTT) were evaluated.

The objective of the study was to examine the pharmacodynamics, pharmacokinetics, and tolerability of sitagliptin. This was a randomized, double-blind, placebo-controlled, 3-period, single-dose crossover study. The study was conducted at 6 investigational sites. The study population consisted of 58 patients with type 2 diabetes who were not on antihyperglycemic agents. Interventions included sitagliptin 25 mg, sitagliptin 200 mg, or placebo. Measurements included plasma DPP-4 activity; post-OGTT glucose excursion; active and total incretin GIP levels; insulin, C-peptide, and glucagon concns.; and sitagliptin pharmacokinetics. Sitagliptin dose-dependently inhibited plasma DPP-4 activity over 24 h, enhanced active GLP-1 and GIP levels, increased insulin/C-peptide, decreased glucagon, and reduced glycemic excursion after OGTTs administered at 2 and 24 h after single oral 25- or 200-mg doses of sitagliptin. Sitagliptin was generally well tolerated, with no hypoglycemic events. In this study in patients with type 2 diabetes, near maximal glucose-lowering efficacy of sitagliptin after single oral doses was associated with inhibition of plasma DPP-4 activity of 80% or greater, corresponding to a plasma sitagliptin concentration of 100 nM or greater, and an augmentation of active GLP-1 and GIP levels of 2-fold or higher after an OGTT.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sitagliptin on incretin and blood glucose levels in patients with type 2 diabetes)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

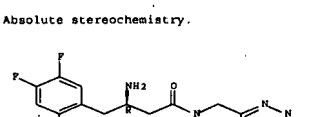


RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 50 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1193860 CAPLUS Full-text
DN 146:242978
TI The incretin system: glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes
AU Drucker, Daniel J.; Nauck, Michael A.
CS Samuel Lunenfeld Research Institute, Mount Sinai Hospital, University of Toronto, Toronto, ON, Can.
SO Lancet (2006), 368(9548), 1696-1705
CODEN: LANCAO; ISSN: 0140-6736
PB Elsevier Ltd.
DT Journal; General Review
LA English
AB A review. Glucagon-like peptide 1 (GLP-1) is a gut-derived incretin hormone that stimulates insulin and suppresses glucagon secretion, inhibits gastric

emptying, and reduces appetite and food intake. Therapeutic approaches for enhancing incretin action include degradation-resistant GLP-1 receptor agonists (incretin mimetics), and inhibitors of dipeptidyl peptidase-4 (DPP-4) activity (incretin enhancers). Clin. trials with the incretin mimetic exenatide (two injections per day or long-acting release form once weekly) and liraglutide (one injection per day) show redns. in fasting and postprandial glucose concns., and Hb A1c (HbA1c) (1-2%), associated with weight loss (2-5 kg). The most common adverse event associated with GLP-1 receptor agonists is mild nausea, which lessens over time. Orally administered DPP-4 inhibitors, such as sitagliptin and vildagliptin, reduce HbA1c by 0·5-1·0%, with few adverse events and no weight gain. These new classes of antidiabetic agents, and incretin mimetics and enhancers, also expand β-cell mass in preclin. studies. However, long-term clin. studies are needed to determine the benefits of targeting the incretin axis for the treatment of type 2 diabetes.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of glucagon-like peptide 1 receptor agonists and dipeptidyl peptidase inhibitor in treating patients with type 2 diabetes)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

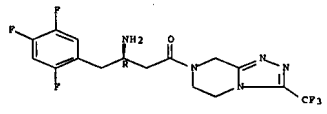


RE.CNT 109 THERE ARE 109 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 51 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1179059 CAPLUS Full-text
DN 146:55218
TI Efficacy and safety of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy in patients with type 2 diabetes mellitus
AU Raz, I.; Hanefeld, M.; Xu, L.; Caria, C.; Williams-Herman, D.; Khatami, H.
CS Diabetes Research Center, Hadassah University Hospital, Jerusalem, Israel
SO Diabetologia (2006), 49(11), 2564-2571
CODEN: DBTGAJ; ISSN: 0012-186X
PB Springer GmbH
DT Journal
LA English
AB Aims/hypothesis: The aim of this study was to assess the efficacy and safety of sitagliptin (MK-0431) as monotherapy in patients with type 2 diabetes mellitus and inadequate glycemic control (HbA1c ≥7% and ≤10%) on exercise and diet. Methods: A total of 521 patients aged 27-76 years with a mean baseline HbA1c of 8.1% were randomized in a 1:2:2 ratio to treatment with placebo, sitagliptin 100 mg once daily, or sitagliptin 200 mg once daily, for 18 wk. The efficacy anal. was based on an all-patients-treated population using an anal. of covariance, excluding data obtained after glycemic rescue. Results:

After 18 wk, HbA1c was significantly reduced with sitagliptin 100 mg and 200 mg compared with placebo (placebo-subtracted HbA1c reduction: -0.60% and -0.48%, resp.). Sitagliptin also significantly decreased fasting plasma glucose relative to placebo. Patients with higher baseline HbA1c (≥9%) experienced greater placebo-subtracted HbA1c redns. with sitagliptin (-1.20% for 100 mg and -1.04% for 200 mg) than those with HbA1c <8% (-0.44% and -0.33%, resp.) or ≥8% to 8.9% (-0.61% and -0.39%, resp.). Homeostasis model assessment beta cell function index and fasting proinsulin:insulin ratio, markers of insulin secretion and beta cell function, were significantly improved with sitagliptin. The incidence of hypoglycemia and gastrointestinal adverse experiences was not significantly different between sitagliptin and placebo. Sitagliptin had a neutral effect on body weight. Conclusions/interpretation: Sitagliptin significantly improved glycemic control and was well tolerated in patients with type 2 diabetes mellitus who had inadequate glycemic control on exercise and diet.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sitagliptin was well tolerated and significantly improved glycemic control in patient with type 2 diabetes mellitus and inadequate glycemic control on exercise and diet)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 52 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1177439 CAPLUS Full-text
DN 145:465736
TI Combination of dipeptidyl peptidase-IV inhibitor and a cannabinoid CB1 receptor antagonist for the treatment of diabetes and obesity
IN Amatruda, John M.; Fong, Tung M.; Moller, David E.; Thornberry, Nancy A.
PA (Merck & Co., Inc., USA
SO PCT Int. Appl., 54pp.
CODEN: PIXXD2
DT Patent
LA English
PAN.CNT 1

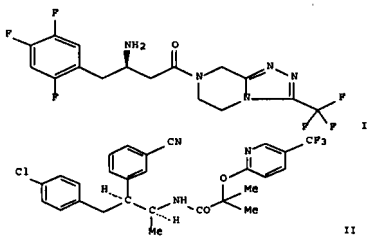
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006119260	A2	20061109	WO 2006-US16754	20060428

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,

KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-676783P P 20050502

GI



I

II

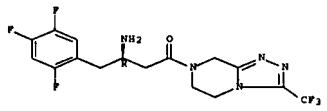
AB The present invention relates to pharmaceutical compns. comprising a combination of a particular dipeptidyl peptidase-IV (DPP-IV) inhibitor (e.g. (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3- a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine dihydrogen phosphate monohydrate; free base shown as I) and a particular cannabinoid CB1 receptor antagonist/inverse agonist (e.g. N-[(1S,2S)-3-(4- chlorophenyl)-2-(3-cyanophenyl)-1-methylpropyl]-2-methyl-2-[[5- (trifluoromethyl)pyridin-2-yl]oxy]propanamide; shown as II), kits containing such combinations and methods of using such compns. for the treatment of diabetes, diabetes associated with obesity, diabetes-related disorders, obesity, and obesity-related disorders (no data). Although the methods of preparation are not claimed, prepns. and/or characterization data for the above examples are included.

IT 486460-32-6P, (2R)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(candidate codrug; combination of dipeptidyl peptidase-IV inhibitor and cannabinoid CB1 receptor antagonist for treatment of diabetes and obesity)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 654671-77-9P, (2R)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine dihydrogen phosphate monohydrate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(candidate codrug; combination of dipeptidyl peptidase-IV inhibitor and cannabinoid CB1 receptor antagonist for treatment of diabetes and obesity)

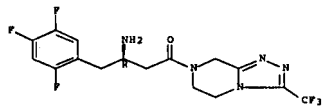
RN 654671-77-9 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

IT 654671-78-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(candidate codrug; combination of dipeptidyl peptidase-IV inhibitor and cannabinoid CB1 receptor antagonist for treatment of diabetes and obesity)

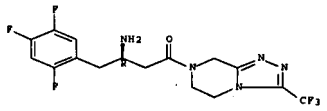
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

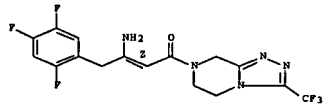
CRN 7664-38-2
CMF H3 O4 P

IT 767340-03-4P, (2Z)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)but-2-en-2-amine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(combination of dipeptidyl peptidase-IV inhibitor and cannabinoid CB1 receptor antagonist for treatment of diabetes and obesity)

RN 767340-03-4 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(2Z)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)-2-butenyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



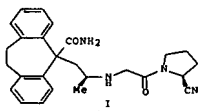
L11 ANSWER 83 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:1147258 CAPLUS Full-text
DN 145:471864
TI Preparation of multicyclic peptide derivatives as dipeptidyl peptidase-IV inhibitors
IN Kroth, Heiko; Feuerstein, Tim; Richter, Frank; Boer, Jurgen; Essers, Michael; Nolte, Bert; Schneider, Matthias; Hochguertel, Matthias; Frickel, Fritz-Frieder; Taveras, Arthur
PA Alantos Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 542pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006116157	A2	20061102	WO 2006-US15200	20060421
	WO 2006116157	A9	20070301		
	WO 2006116157	A3	20070419		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

	US 2006270701	A1	20061130	US 2006-409481	20060421

PRAI US 2005-674151P P 20050422
OS CASREACT 145:471864; MARPAT 145:471864
GI



I

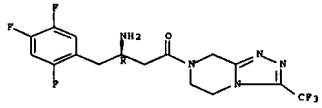
AB The invention relates generally to pyrrolidine and thiazolidine DPP-IV inhibitory compds. A-B-CO-D (A is a bicyclic or tricyclic ring system attached to B at carbon or nitrogen; B is a linking group such as an amino acid residue or fragment; D is a pyrrolidine or thiazolidine residue or derivative), including isomers and pharmaceutically-acceptable salts, for treatment of DPP-IV mediated diseases, in particular, type-2 diabetes. Thus, pyrrolidinecarbonitrile derivative I was prepared by reaction of 5-[(S)-2-aminopropyl]-10,11-dihydro-5H-dibenzo[a,d]cycloheptene-5- carboxamide with N-glyoxyloyl-L-prolinecarbonitrile (prepns. given) and showed Ki < 6 nM for inhibition of DPP-IV.

IT 486460-32-6, Sitagliptin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of multicyclic peptide derivs. as dipeptidyl peptidase-IV inhibitors)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-. (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 54 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:952876 CAPLUS Full-text
DN 145:328380
TI Combination therapy for endothelial dysfunction, angina and diabetes
IN Kaesemeyer, Wayne
PA USA
SO U.S. Pat. Appl. Publ., 14pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2006205727	A1	20060914	US 2006-373658	20060310
WO 2006099244	A1	20060921	WO 2006-US8801	20060310

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-660625P P 20050311
US 2005-675118P P 20050427

AB The combination of a HMG CoA reductase inhibitor like a statin, such as simvastatin, with a pFox inhibitor such as trimetazidine ("Simetazidine") is particularly advantageous for treatment of end-stage complications, such as acute coronary syndrome (ACS) and chronic angina, especially in type II diabetics. The combination therapy is also useful in the treatment and/or prevention of chronic heart failure (CHF) and peripheral arterial disease (PAD). The combination of a nitric oxide (NO) mechanism with increased NO production with pFox inhibition simultaneously treats both the effect and the cause of angina. One or more oral hypoglycemic compds. (biguanides, insulin sensitizers, such as thiazolidinediones, α-glucosidase inhibitors, insulin secretagogues, and dipeptidyl peptidase IV inhibitors), protein kinase C (PKC) inhibitors, and acetyl-CoA carboxylase inhibitors can also be used in combination with the HMG CoA reductase inhibitors and/or pFox inhibitors, especially in type II diabetics, to control glucose levels and treat endothelial dysfunction. The drugs can be given in combination (e.g. a single tablet) or in sep. dosage forms, administered simultaneously or sequentially. In the preferred form the statin is given in a dose of between 5 and 80 mg/day in two sep. doses, and the pFox inhibitor is administered in a sustained or extended dosage formulation at a dose of 20 mg three times a day or 35 mg two times a day. The dose of the oral hypoglycemic, PKC inhibitor, or acetyl-CoA carboxylase inhibitor varies with the type of drug used.

IT 654671-78-0, MK 431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for endothelial dysfunction, angina and diabetes)

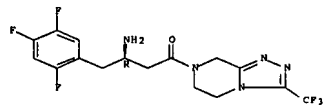
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 55 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:945768 CAPLUS Full-text
DN 145:328394
TI Roflumilast for the treatment of diabetes mellitus
IN Kley, Hans-Peter; Hanauer, Guido; Hauser, Daniela; Schmidt, Beate; Bredenbroeker, Dirk; Wurst, Wilhelm; Kemkowski, Joerg
PA Altana Pharma AG, Germany
SO PCT Int. Appl., 67pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006094942	A1	20060914	WO 2006-EP60445	20060303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI EP 2005-101780 A 20050308

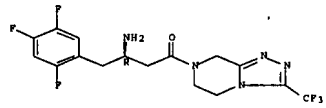
AB The invention discloses the use of Roflumilast and/or Roflumilast-N-Oxide for the treatment of diabetes mellitus and accompanying disorders thereof. The invention addnl. discloses combinations of Roflumilast and/or Roflumilast-N-Oxide with other active agents for the treatment of diabetes mellitus.

IT 486460-32-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Roflumilast for treatment of diabetes mellitus and accompanying disorders, and combinations with other agents)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 56 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:944442 CAPLUS Full-text
DN 145:328392
TI Roflumilast for the treatment of diabetes mellitus and accompanying disorders, and combinations with other agents
IN Kley, Hans-Peter; Hanauer, Guido; Hauser, Daniela; Schmidt, Beate; Bredenbroeker, Dirk; Wurst, Wilhelm; Kemkowski, Joerg
PA Altana Pharma AG, Germany
SO PCT Int. Appl., 71pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006094933	A1	20060914	WO 2006-EP60418	20060303
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRAI EP 2005-101772 A 20050308

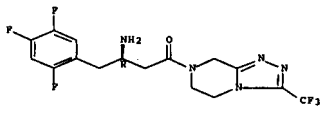
AB The invention relates to the use of Roflumilast and/or Roflumilast-N-Oxide for the treatment of diabetes mellitus and accompanying disorders thereof. The invention addnl. relates to combinations of Roflumilast and/or Roflumilast-N-Oxide with other active agents for the treatment of diabetes mellitus.

IT 486460-32-6, SITAGLIPTIN
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Roflumilast for treatment of diabetes mellitus and accompanying disorders, and combinations with other agents)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

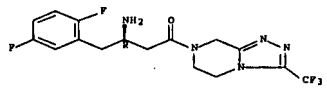
Absolute stereochemistry.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 57 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:930335 CAPLUS Full-text
DN 146:330487
TI Inhibition of dipeptidyl-peptidase IV does not increase circulating IGF-1 concentrations in growing pigs
AU Faidley, T. D.; Leiting, B.; Pryor, K. D.; Lyons, K.; Hickey, G. J.; Thompson, D. R.
CS Department of Pharmacology, Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Experimental Biology and Medicine (Maywood, NJ, United States) (2006), 231(8), 1373-1378
CODEN: EBMMBE; ISSN: 1535-3702
PB Society for Experimental Biology and Medicine
DT Journal
LA English
AB The enzyme dipeptidyl peptidase-IV (DPP-IV) inactivates a variety of bioactive peptides, including glucagon-like peptide-1 (GLP-1) and growth hormone releasing hormone (GHRH). Inhibiting DPP-IV to increase circulating GLP-1 is of interest as a treatment for Type II diabetes. Inactivation of DPP-IV may also increase circulating GHRH, potentially enhancing growth in domestic animals. To test the hypothesis that inhibition of DPP-IV activity will influence the growth hormone/IGF-1 axis, growing swine (Sus scrofa domesticus, 78 kg) were treated with a DPP-IV inhibitor (Compound 1, the 2,5-difluorophenyl analog of the triazolopiperazine MK0431, sitagliptin), and blood plasma concns. of IGF-1 were monitored. Swine were administered either sterile saline (0.11 mL/kg followed by a continuous infusion at 2 mL/h for 72 h, controls, n = 2), Compound 1 (2.78 mg/kg followed by a continuous infusion at 0.327 mg/kg·hr for 72 h, n = 4) or GHRH (0.11 mL/kg sterile saline, followed by a continuous infusion of GHRH at 2.5 μg/kg·hr for 48 h, n = 4). Plasma concns. of Compound 1 were maintained at 1 μM, which resulted in a 90% inhibition of circulating DPP-IV activity. Relative to the predose 24-h period, area under the IGF-1 concentration curve (AUC) tended to be lower with Compound 1 (-79 ng/mL·hr) than controls (543 ng/mL·hr). GHRH treatment increased the IGF-1 AUC (1210 ng/mL·hr). We conclude that inhibition of DPP-IV does not alter the circulating levels of IGF-1 in the growing swine.
IT 486460-31-5
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of dipeptidyl-peptidase IV does not increase circulating IGF-1 concns. in growing swine)
RN 486460-31-5 CAPLUS
CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

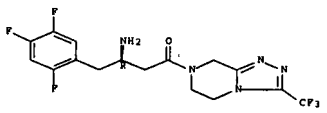


RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 58 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:903209 CAPLUS Full-text
DN 146:54398
TI Sitagliptin: a dipeptidyl peptidase IV inhibitor for the treatment of type 2 diabetes
AU Miller, Shannon A.; St. Onge, Erin L.
CS Pharmacotherapy Faculty, Florida Hospital Family Practice Residency, Orlando, FL, USA
SO Annals of Pharmacotherapy (2006), 40(7/8), 1336-1343
CODEN: APHRER; ISSN: 1060-0280
PB Harvey Whitney Books Co.
DT Journal; General Review
LA English
AB Objective: To review the pharmacol., pharmacokinetics, safety, and efficacy of sitagliptin, a dipeptidyl peptidase IV (DPP-IV) inhibitor in the management of type 2 diabetes mellitus. Data Sources: A MEDLINE search (1966-Feb. 2006) was conducted for English-language articles using the terms dipeptidyl peptidase IV inhibitor, incretin, MK-0431, and sitagliptin. Abstrs. from the American Diabetes Association annual meetings in 2004 and 2005 were included as sources of data. Study Selection And Data Extraction: Articles pertaining to the pharmacol. of sitagliptin, its pharmacokinetics, safety and efficacy were reviewed. Data Synthesis: Sitagliptin is a potent, competitive, reversible inhibitor of the DPP-IV enzyme. It is eliminated renally, with a terminal half-life of 11.8-14.4 h. In Phase II clin. trials, sitagliptin was found to be superior to placebo for the treatment of type 2 diabetes mellitus. Results of a small trial comparing sitagliptin with glipizide indicate that both treatments are comparable. The efficacy of sitagliptin has also been demonstrated when used as adjunctive therapy with metformin. Few adverse effects have been reported. Weight gain and hypoglycemia have not been seen with sitagliptin therapy. Conclusions: Based on its unique mechanism of action, sitagliptin will provide practitioners with an addnl. tool in the treatment of diabetes. Review of the literature to date implies sitagliptin may be effective as monotherapy in type 2 diabetes. In addition, existing evidence supports the use of sitagliptin as adjunct therapy to sulfonylureas and metformin. Another advantage of sitagliptin use is that it appears to be free from the adverse effects of weight gain and hypoglycemia that are associated with currently available treatments.
IT 486460-32-6, Sitagliptin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sitagliptin as monotherapy and as adjunct therapy with sulfonylurea and metformin was effective without any adverse effects of weight gain and

hypoglycemia in type 2 diabetes mellitus patient)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

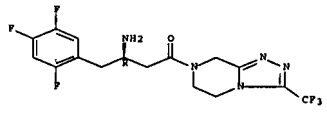


RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 59 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:826044 CAPLUS Full-text
DN 146:176805
TI Pharmacokinetics and pharmacodynamic effects of the oral DPP-4 inhibitor sitagliptin in middle-aged obese subjects
AU Herman, Gary A.; Bergman, Arthur; Liu, Fang; Stevens, Cathy; Wang, Amy Q.; Zeng, Wei; Chen, Li; Snyder, Karen; Hilliard, Deborah; Tanen, Michael; Tanaka, Wesley; Meehan, Alan G.; Lasseter, Kenneth; Dilzer, Stacy; Blum, Robert; Wagner, John A.
CS Merck Research Laboratories, Rahway, NJ, USA
SO Journal of Clinical Pharmacology (2006), 46(8), 876-886
CODEN: JCPCBR; ISSN: 0091-2700
PB Sage Publications
DT Journal
LA English
AB Sitagliptin (MK-0431) is an oral, potent, and selective dipeptidyl peptidase-IV (DPP-4) inhibitor developed for the treatment of type 2 diabetes. This multicenter, randomized, double-blind, placebo-controlled study examined the pharmacokinetic and pharmacodynamic effects of sitagliptin in obese subjects. Middle-aged (45-63 years), nondiabetic, obese (body mass index: 30-40 kg/m2) men and women were randomized to sitagliptin 200 mg bid (n = 24) or placebo (n = 8) for 28 days. Steady-state plasma concns. of sitagliptin were achieved within 2 days of starting treatment, and >90% of the dose was excreted unchanged in urine. Sitagliptin treatment led to .apprx.90% inhibition of plasma DPP-4 activity, increased active glucagon-like peptide-1 (GLP-1) levels by 2.7-fold (P <.001), and decreased post-oral glucose tolerance test glucose excursion by 35% (P <.050) compared to placebo. In non-diabetic obese subjects, treatment with sitagliptin 200 mg bid was generally well tolerated without associated hypoglycemia and led to maximal inhibition of plasma DPP-4 activity, increased active GLP-1, and reduced glycemic excursion.
IT 486460-32-6, Sitagliptin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sitagliptin inhibits of plasma dipeptidyl peptidase-IV activity, increased active glucagon-like peptide-1 levels and decreased glucose excursion in middle-aged obese patient with diabetes)
RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

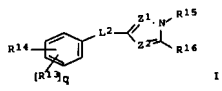


RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

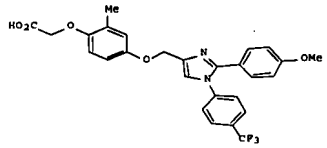
L11 ANSWER 60 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:795736 CAPLUS Full-text
DN 145:230633
TI Preparation of 4-[(benzimidazolyl/pyrazolyl/triazolyl)methoxy]phenoxyaceti c acids as PPAR modulators
IN Cow, Christopher; Epple, Robert; Wang, Xing; Xie, Yongping
PA Irm LLC, Bermuda
SO PCT Int. Appl., 62pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006084176	A2	20060810	WO 2006-US3924	20060203
WO 2006084176	A3	20060914		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI US 2005-649962P	P	20050203		

OS MARPAT 145:230633
GI



I



II

AB The title compds. I [q = 0-3; Z1, Z2 = CH, N; L2 = XOX, XSOO-2X, XSOO-2XO (wherein X = a bond, (un)substituted alkylene); R13 = halo, alkyl, alkoxy, etc.; R14 = XOXC(O)OR17, XC(O)OR17 (X = a bond, alkylene; R17 = H, alkyl); R15, R16 = R18 or YR18 (Y = alkylene, alkenylene, alkynylene, CONR17, OX; X = a bond, alkylene; R17 = H, alkyl; R18 = cycloalkyl, heterocycloalkyl, aryl, heteroaryl); or R15 and R16 together with the atoms to which R15 and R16 are attached form fused bicyclic or tricyclic heteroaryl], useful in treating or preventing diseases or disorders associated with the activity of the peroxisome proliferator-activated receptor (PPAR) families, particularly the activity of PPARδ (no specific data given), were prepared Thus, reacting Me (4-hydroxy-2-methylphenoxy)acetate with 4-(chloromethyl)-2-(4-methoxyphenyl)-1-(4-trifluoromethylphenyl)-1H- imidazole (prepns. given) followed by hydrolysis afforded 28% II. Also disclosed are pharmaceutical compns. comprising compds. I alone or in combination with other therapeutic agents.

IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 4-[(benzimidazolyl/pyrazolyl/triazolyl)methoxy]phenoxyacetic acids as PPAR modulators for treating and preventing diseases-associated with PPAR activity, particularly activity of PPARδ)

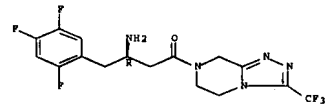
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 61 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:768357 CAPLUS Full-text
DN 145:189177
TI Process for the preparation of chiral β-amino acid derivatives by asymmetric hydrogenation of enamino esters and amides using transition metal-complexed chiral ferrocenyldiphosphines
IN Xiao, Yi; Armstrong, Joseph D., III; Krska, Shane W.; Njolito, Eugenia; Rivera, Nelo R.; Sun, Yongkui; Rosner, Thorsten; Clausen, Andrew M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 27pp.
CODEN: PIXXD2
DT Patent
LA English
PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006081151	A1	20060803	WO 2006-US2147	20060120

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRAI US 2005-646697P P 20050124
OS MARPAT 145:189177

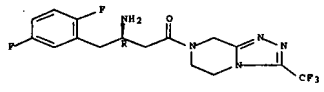
AB The invention relates to a process for the efficient preparation of enantiomerically enriched β-amino acid derivs. R1CH(NH2)CH2CO-Z [Z = OR2, SR2, NR2R3; R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2, R3 = H, alkyl, aryl, aralkyl; R2R3N = (substituted) 4-7 membered ring] having (R)- or (S)-configuration which are useful in the asym. synthesis of biol. active mols. The process comprises an enantioselective hydrogenation of a prochiral β-aminoacrylic acid derivative in the presence of an ammonium salt and a transition metal precursor complexed with a chiral ferrocenyl diphosphine ligand. Thus, (Z)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)but-2-en-2-amine (preparation given) was hydrogenated in the presence of chloro(1,5-cyclooctadiene)rhodium(I) dimer, (R,S) tert-Bu Josiphos, and ammonium chloride in MeOH at 100 psi and 50 °C for 18 h to give 97% (R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine in 98-99% enantiomeric excess.

IT 486460-31-5P 486460-32-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of chiral β-amino acid derivs. by asym. hydrogenation of enamino esters and amides using transition metal-complexed chiral ferrocenyldiphosphines)

RN 486460-31-5 CAPLUS

CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

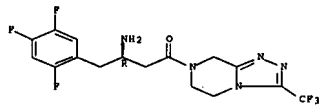
Absolute stereochemistry.



RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



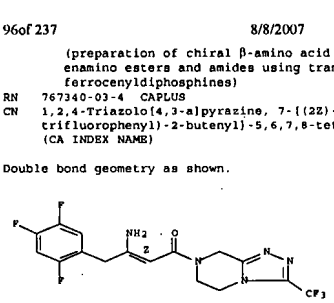
IT 767340-03-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of chiral β-amino acid derivs. by asym. hydrogenation of enamino esters and amides using transition metal-complexed chiral ferrocenyldiphosphines)

RN 767340-03-4 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(2Z)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)-2-butenyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 62 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:761925 CAPLUS Full-text
DN 145:201985
TI Discovery, Structure-Activity Relationship, and Pharmacological Evaluation of (5-Substituted-pyrrolidinyl-2-carbonyl)-2-cyanopyrrolidines as Potent Dipeptidyl Peptidase IV Inhibitors. [Erratum to document cited in CA145:116704]
AU Pei, Zhonghua; Li, Xiaofeng; Longenecker, Kenton; von Geldern, Thomas W.; Wiedeman, Paul E.; Lubben, Thomas H.; Zinker, Bradley A.; Stewart, Kent; Ballaron, Stephen J.; Stashko, Michael A.; Mika, Amanda K.; Beno, David W. A.; Long, Michelle; Wells, Heidi; Kempf-Grote, Anita J.; Madar, David J.; McDermott, Todd S.; Bhagavatula, Lakshmi; Fickes, Michael G.; Pireh, Daisy; Solomon, Larry R.; Lake, Marc R.; Edalji, Rohinton; Fry, Elizabeth H.; Sham, Hing L.; Trevillyan, James M.
CS Metabolic Disease Research, Advanced Technology, Departments of Exploratory Pharmacokinetics and Pharmaceutics and Process Chemistry Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA
SO Journal of Medicinal Chemistry (2006), 49(17), 5387
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB On page 3521, right column, "Results and Discussion" section, last paragraph, the last line is missing the words "then the C5-position" before "...of the P2 pyrrolidine ring...". With the added words, the correct sentence is "Alternatively, upon analyzing the structures of more potent inhibitors, cyanopyrrolidine 2 (Chart 1) and compound 10a, it occurred to us that if the P2 pyrrolidine moiety of compound 10a, it occurred to us that if the P2 pyrrolidine moiety of compound 10a could serve as a rigidified linker to replace the flexible aminino side chain of cyanopyrrolidine 2, then the C5-position of the P2 pyrrolidine ring could be modified to improve potency and other properties.".

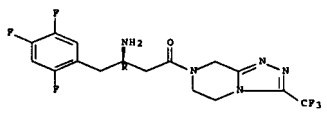
IT 654671-78-0, MK 0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(Discovery, Structure-Activity Relationship, and Pharmacol. Evaluation of (5-Substituted-pyrrolidinyl-2-carbonyl)-2-cyanopyrrolidines as Potent Dipeptidyl (Erratum))
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 63 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:733033 CAPLUS Full-text
DN 145:174316
TI Direct compression formulation comprising dipeptidylpeptidase IV inhibitor
IN Pfeffer, Sabine; Schaefer, Frank; Schneeberger, Ricardo; Sutton, Paul Allen; Trueby, Martin Friedrich; Wirth, Wolfgang
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006078593	A2	20060727	WO 2006-US1473	20060117
	WO 2006078593	A3	20060914		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

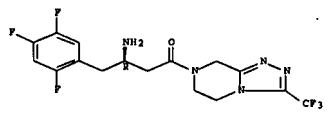
	AU 2006206670	A1	20060727	AU 2006-206670	20060117
	US 2006210627	A1	20060921	US 2006-333582	20060117
PRAI	US 2005-644645P	P	20050118		
	US 2005-690484P	P	20050614		
	WO 2006-US1473	W	20060117		

AB This invention relates to tablets especially tablets formed by direct compression of a dipeptidylpeptidase IV (DPP-IV) inhibitor compound, a process for the preparation thereof, to new pharmaceutical formulations, and new tableting powders comprising DPP-IV inhibitor formulations capable of being directly compressed into tablets. The invention relates further to a process for preparing the tablets by blending the active ingredient and specific excipients into the new formulations and then directly compressing the formulations into the direct compression tablets. The invention also relates to vildagliptin particle size distribution and a new crystal form of vildagliptin particularly adapted for the preparation of improved tablets and other pharmaceutical compns. For example, tablets were produced containing LAF237 100 mg , microcryst. cellulose 191,36 mg, lactose anhydrous 95.64 mg, sodium starch glycolate 8 mg and magnesium stearate 5 mg.
IT 654671-78-0, MK-0431
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(direct compression formulation comprising dipeptidylpeptidase IV inhibitor)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

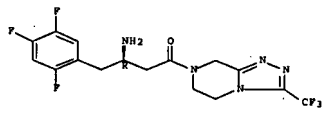
CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 64 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:681434 CAPLUS Full-text
DN 145:137853
TI Pharmaceutical compositions and methods using a biological response modifier and a β-cell growth factor for restoring β-cell mass and function
IN Nadler, Jerry
PA Diakine Therapeutics, Inc., USA
SO PCT Int. Appl., 121 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006074051	A2	20060713	WO 2005-US47390	20051230
	WO 2006074051	A3	20061109		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	US 2006160736	A1	20060720	US 2005-321090	20051230
PRAI	US 2004-640523P	P	20041230		
OS	MARPAT 145:137853				

AB Pharmaceutical compns. and methods for using are provided for restoring β-cell mass and function in a mammal in need thereof. The pharmaceutical compns. have a biol. response modifier and a β-cell growth factor in admixt. with a pharmaceutically acceptable carrier, adjuvant or vehicle. The compns. of the invention may be used to treat diabetes.
IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biol. response modifier and β-cell growth factor for restoring β-cell mass and function)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 65 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:677805 CAPLUS Full-text
DN 145:137850
TI Combination therapy for diabetes and related disorders using a GPR119 agonist and dipeptidyl peptidase IV inhibitor for lowering blood glucose and increasing GLP-1 levels
IN Chu, Zhi-Liang; Leonard, James N.; Al-Shamma, Hussien A.; Jones, Robert M.
PA USA
SO U.S. Pat. Appl. Publ., 99 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2006154866	A1	20060713	US 2006-328405	20060109
	WO 2006076231	A2	20060720	WO 2006-US510	20060109
	WO 2006076231	A3	20070118		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	EP 1758565	A2	20070307	EP 2006-717678	20060109
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	EP 1808168	A1	20070718	EP 2007-4743	20060109
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
	US 2007072803	A1	20070329	US 2006-603410	20061122
	US 2007072804	A1	20070329	US 2006-603417	20061122
PRAI	US 2005-643086P	P	20050110		
	US 2005-683172P	P	20050519		
	US 2005-726880P	P	20051014		

EP 2006-717678 A3 20060109
US 2006-328405 A1 20060109
WO 2006-US510 W 20060109

AB The present invention provides combination of a G protein-coupled receptor GPR119 agonist with a dipeptidyl peptidase IV (DPP-IV) inhibitor such that the combination provides an effect in lowering a blood glucose level or in increasing a blood GLP-1 level in a subject for treating or preventing diabetes and other related conditions. The present invention also relates to the use of a G protein-coupled receptor to screen for GLP-1 secretagogues. GPR119 agonist is AR231453 while DPP-IV inhibitors of the invention include MK-0431, LAF237 and PE107542.

IT 654671-78-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DPP-IV inhibitor; combination therapy for diabetes and related disorders using GPR119 agonist and dipeptidyl peptidase IV inhibitor for lowering blood glucose and increasing GLP-1 levels)

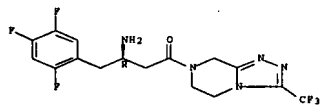
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 66 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:639624 CAPLUS Full-text
DN 145:465116

TI Pharmacokinetic and pharmacodynamic properties of multiple oral doses of sitagliptin, a dipeptidyl peptidase-IV inhibitor: a double-blind, randomized, placebo-controlled study in healthy male volunteers

AU Bergman, Arthur J.; Stevens, Catherine; Zhou, YanYan; Yi, Bingming; Laethem, Martine; De Smet, Marina; Snyder, Karen; Hilliard, Deborah; Tanaka, Wesley; Zeng, Wei; Tanen, Michael; Wang, Amy Q.; Chen, Li; Winchell, Gregory; Davies, Michael J.; Ramael, Steven; Wagner, John A.; Herman, Gary A.

CS Merck & Co., Inc., Whitehouse Station, NJ, USA

SO Clinical Therapeutics (2006), 28(1), 55-72
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English

AB Background: Dipeptidyl peptidase-IV (DPP-IV) inhibitors represent a new class of oral antihyperglycemic agents. Sitagliptin is an orally active and selective DPP-IV inhibitor currently in Phase III development for the treatment of type 2 diabetes mellitus. Objective: The aim of this study was to assess the pharmacokinetic and pharmacodynamic (PK/PD) properties and tolerability of multiple oral once-daily or twice-daily doses of sitagliptin. Methods: This double-blind, randomized, placebo-controlled, incremental oral-dose study was conducted at SGS Biopharma, Antwerp, Belgium. Healthy, nonsmoking male volunteers aged 18 to 45 years with a creatinine clearance rate of >80 mL/min and normoglycemia and weighing within 15% of their ideal height/weight range were randomly assigned to 1 of 8 treatment groups: sitagliptin 25, 50, 100, 200, or 400 mg or placebo, QD for 10 days; a single dose of sitagliptin 800 mg administered on day 1 followed by 600 mg QD on days 3 to 10; or sitagliptin 300 mg BID for 10 days. For anal. of PK properties, plasma and urine samples were obtained before study drug administration on day 1 and at 0.5, 1, 2, 4, 6, 8, 10, 12, and 16 h after study drug administration on day 1; before study drug administration on days 2 to 9; and every 24 h for 96 h after the last dose on day 10, and analyzed for sitagliptin concns. Assays were used to measure inhibition of plasma DPP-IV activity and plasma concns. of active and total glucagon-like peptide-1 (GLP-1), glucose, and glucagon, and serum concns. of insulin, C-peptide, insulin-like growth factor-1, and insulin-like growth factor binding protein-3. Tolerability was assessed throughout the study using phys. examination, including vital sign measurements; 12-lead electrocardiog.; and laboratory anal., including hematol., biochem. (hepatic aminotransferase and creatine phosphokinase), and urinalysis. Results: Seventy subjects were enrolled (mean age, 32.9 years [range, 18-45 years]; mean weight, 79.7 kg [range, 63.4-97.7 kg]; 8 patients per sitagliptin study group and 14 patients in the control group). In the sitagliptin groups, the plasma concentration-time profiles and principal PK parameters (Tmax, Cmax, and t1/2) were statistically similar at days 1 (single dose) and 10 (steady state). In the groups receiving sitagliptin QD doses, accumulation of sitagliptin was modest (AUC accumulation ratio [day 10/day 1] range, 1.05-1.29), and the apparent terminal elimination t1/2 was 11.8 to 14.4 h. At steady state in the sitagliptin QD groups, the mean proportion of drug excreted unchanged in the urine was .apprx.70.6%. Dose-dependent inhibition of plasma DPP-IV activity was apparent, and the pattern of inhibition at steady state (day 10) was statistically similar to that observed on day 1. Day-10 weighted mean inhibition of plasma DPP-IV activity over 24 h was ≥80% for doses of ≥50 mg QD. After a standard meal, active GLP-1 concns. were significantly increased in the sitagliptin groups by .apprx.2-fold compared with that in the control group, a finding consistent with near-maximal acute glucose lowering in preclin. studies. Across doses, no apparent adverse effects, including hypoglycemia, were found or reported. Conclusions: The results from this study in a select population of healthy male volunteers suggest that multiple oral doses of sitagliptin inhibited plasma DPP-IV activity and affected active GLP-1 concns. in a dose-dependent manner, without

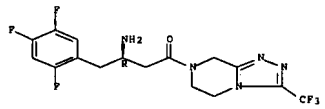
producing hypoglycemia. Multiple dosing of sitagliptin exhibited a PK/PD profile consistent with that of a QD regimen and was well tolerated.

IT 486460-32-6, Sitagliptin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase-IV inhibitor sitagliptin revealed modest pharmacokinetic profile, inhibited plasma dipeptidyl peptidase-IV and was well tolerated in human)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 67 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:559882 CAPLUS Full-text
DN 145:284727
TI Chronic inhibition of dipeptidyl peptidase-4 with a sitagliptin analog preserves pancreatic β-cell mass and function in a rodent model of type 2 diabetes

AU Mu, James; Woods, John; Zhou, Yun-Ping; Roy, Ranabir Sinha; Li, Zhihua; Zycband, Emanuel; Feng, Yue; Zhu, Lan; Li, Cai; Howard, Andrew D.; Moller, David E.; Thornberry, Nancy A.; Zhang, Bei B.

CS Department of Metabolic Disorders, Merck Research Laboratories, Rahway, NJ, USA

SO Diabetes (2006), 55(6), 1695-1704
CODEN: DIAEAZ; ISSN: 0012-1797
PB American Diabetes Association
DT Journal
LA English

AB Inhibitors of dipeptidyl peptidase-4 (DPP-4), a key regulator of the actions of incretin hormones, exert antihyperglycemic effects in type 2 diabetic patients. A major unanswered question concerns the potential ability of DPP-4 inhibition to have beneficial disease-modifying effects, specifically to attenuate loss of pancreatic β-cell mass and function. Here, we investigated the effects of a potent and selective DPP-4 inhibitor, an analog of sitagliptin (des-fluoro-sitagliptin), on glycemic control and pancreatic β-cell mass and function in a mouse model with defects in insulin sensitivity and secretion, namely high-fat diet (HFD) streptozotocin (STZ)-induced diabetic mice. Significant and dose-dependent correction of postprandial and fasting hyperglycemia, HbA1c, and blood plasma triglyceride and free fatty acid levels were observed in HFD/STZ mice following 2-3 mo of chronic therapy. Treatment with des-fluoro-sitagliptin dose dependently increased the number of insulin-pos. β-cells in islets, leading to the normalization of β-cell mass and β-cell-to-α-cell ratio. In addition, treatment of mice with des-fluoro-

sitagliptin, but not glipizide, significantly increased islet insulin content and improved glucose-stimulated insulin secretion in isolated islets. These findings suggest that DPP-4 inhibitors may offer long-lasting efficacy in the treatment of type 2 diabetes by modifying the courses of the disease.

IT 837430-23-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase-4 inhibition and pancreatic β-cell mass and function)

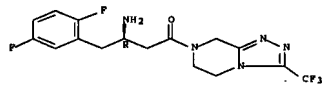
RN 837430-23-6 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-31-5
CMF C16 H16 F5 N5 O

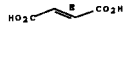
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 68 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:479718 CAPLUS Full-text
DN 145:145648
TI Identification of Ammonium Chloride as an Effective Promoter of the Asymmetric Hydrogenation of a β-Enamine Amide

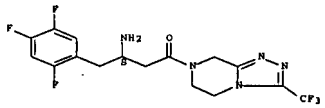
AU Clausen, Andrew M.; Dziadul, Brianne; Cappuccio, Kristine L.; Kaba, Mahmoud; Starbuck, Cindy; Hsiao, Yi; Dowling, Thomas M.

CS Process Research Development (Process Research), Merck & Co., Inc., Rahway, NJ, 07065, USA

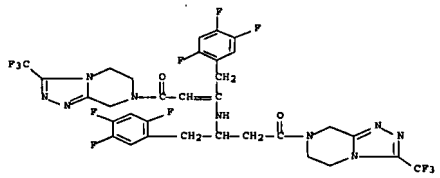
SO Organic Process Research & Development (2006), 10(4), 723-726
CODEN: OPRDFK; ISSN: 1083-6160

PB American Chemical Society
DT Journal
LA English
OS CASREACT 145:145648
AB An investigation into the cause of substrate-specific hydrogenation performance variability was conducted. A significant and unexpected correlation was observed between apparent pH of a solution of the substrate and rate of conversion and enantioselectivity. This observation led to the examination of low and variable levels of native ammonium chloride in different lots of substrate. The presence of ammonium chloride was found to have a pos. effect on reaction rate and enantioselectivity when controlled within a relatively narrow range. Optimal performance was achieved with a mole ratio of 1:1 ammonium chloride to catalyst. The enamine amide, 7-[3-amino-1-oxo-4-(2,4,5-trifluorophenyl)-2-butenyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine, was converted to stigaliptin.
IT 823817-55-6P, (S)-Sitagliptin 898543-70-9P
RL: BYP (Byproduct); PREP (Preparation)
(ammonium chloride as effective promoter of substrate-specific, stereoselective hydrogenation of stigaliptin precursor [amino(oxo)(trifluorophenyl)butenyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine)
RN 823817-55-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3S)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

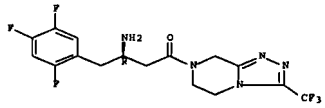


RN 898543-70-9 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[3-[[3-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]-1-propenyl]amino]-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

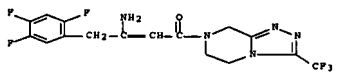


IT 486460-32-6P, Sitagliptin
RL: SPN (Synthetic preparation); PREP (Preparation)
(ammonium chloride as effective promoter of substrate-specific, stereoselective hydrogenation of stigaliptin precursor [amino(oxo)(trifluorophenyl)butenyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 847445-81-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(ammonium chloride as effective promoter of substrate-specific, stereoselective hydrogenation of β-enamine amide)
RN 847445-81-2 CAPLUS
CN 2-Buten-1-one, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)- (CA INDEX NAME)



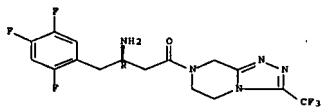
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 69 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:456711 CAPLUS Full-text
DN 145:116704
TI Discovery, Structure-Activity Relationship, and Pharmacological Evaluation of (5-Substituted-pyrrolidinyl-2-carbonyl)-2-cyanopyrrolidines as Potent Dipeptidyl Peptidase IV Inhibitors
AU Pei, Zhonghua; Li, Xiaofeng; Longenecker, Kenton; Von Geldern, Thomas W.; Wiedeman, Paul E.; Lubben, Thomas H.; Zinker, Bradley A.; Stewart, Kent; Ballaron, Stephen J.; Stashko, Michael A.; Mika, Amanda K.; Beno, David W. A.; Long, Michelle; Wells, Heidi; Kempf-Grote, Anita J.; Madar, David J.; McDermott, Todd S.; Bhagavatula, Lakshmi; Fickes, Michael G.; Pireh, Daisy; Solomon, Larry R.; Lake, Marc R.; Edalji, Rohinton; Fry, Elizabeth H.; Sham, Hing L.; Trevillyan, James M.
CS Metabolic Disease Research, Advanced Technology, Departments of Exploratory Pharmacokinetics and Pharmaceutics and Process Chemistry Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL, 60064-3500, USA
SO Journal of Medicinal Chemistry (2006), 49(12), 3520-3535
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 145:116704
AB A series of (5-substituted pyrrolidinyl-2-carbonyl)-2-cyanopyrrolidine (C5-Pro-Pro) analogs was discovered as dipeptidyl peptidase IV (DPPIV) inhibitors as a potential treatment of diabetes and obesity. X-ray crystallog. data show that these inhibitors bind to the catalytic site of DPPIV with the cyano group forming a covalent bond with the serine residue of DPPIV. The C5-substituents make various interactions with the enzyme and affect potency, chemical stability, selectivity, and PK properties of the inhibitors. Optimized analogs are extremely potent with subnanomolar Ki's, are chemical stable, show very little potency decrease in the presence of plasma, and exhibit more than 1,000-fold selectivity against related peptidases. The best compds. also possess good PK and are efficacious in lowering blood glucose in an oral glucose tolerance test in ZDF rats.
IT 654671-78-0, MK 0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Discovery, Structure-Activity Relationship, and Pharmacol. Evaluation of (5-Substituted-pyrrolidinyl-2-carbonyl)-2-cyanopyrrolidines as Potent Dipeptidyl)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

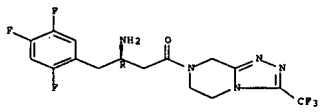
RE.CNT 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 70 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:411999 CAPLUS Full-text
DN 144:456512
TI Combination of DPP-IV inhibitor, PPAR antidiabetic and metformin
IN Burkey, Bryan; Hughes, Thomas Edward
PA Novartis A.-G., Switz.; Novartis Pharma GmbH
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006047248	A1	20060504	WO 2005-US37819	20051021
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2005299808	A1	20060504	AU 2005-299808	20051021
	CA 2581298	A1	20060504	CA 2005-2581298	20051021
	EP 1807066	A1	20070718	EP 2005-816082	20051021
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
PRAI US 2004-621891P P 20041025
WO 2005-US37819 W 20051021
OS MARPAT 144:456512
AB The invention relates to a combination, such as a combined preparation or pharmaceutical composition comprising (1) a dipeptidyl peptidase IV (DPP-IV) inhibitor, (2) one antidiabetic selected from thiazolidinediones (glitazones), non-glitazone type PPAR agonists, PPARα agonists or dual PPARγ/PPARα agonists, and (3) metformin, for simultaneous, sep. or sequential use, especially in the prevention, delay of progression or treatment of conditions mediated by DPP-IV, in particular diabetes, more particularly type 2 diabetes mellitus, conditions of impaired glucose tolerance (IGT), conditions of impaired fasting plasma glucose, metabolic acidosis, ketosis, arthritis, obesity and osteoporosis. The invention also relates to the use of such combination for the preparation of a pharmaceutical preparation for the prevention, delay of progression or treatment of such conditions and for the cosmetic treatment of a mammal in order to effect a cosmetically beneficial loss of body weight; to a method of prevention, delay of progression or treatment of conditions mediated by DPP-IV; and to a method of improving the bodily appearance of a warm-blooded animal. For example, bilayered tablets comprising metformin 500 mg in one layer and the DPP-IV inhibitor 50 mg plus pioglitazone HCl 39.672 (equivalent to 30 mg pioglitazone) in another layer were prepared
IT 486460-32-6 654671-78-0, MK-0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of DPP-IV inhibitor, PPAR agonist and metformin for treatment of metabolic disorders)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

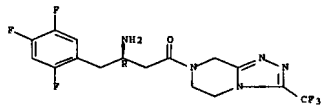


RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

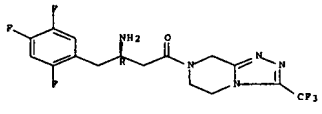
L11 ANSWER 71 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:404434 CAPLUS Full-text
DN 145:55290
TI Determination of MK-0431 in human plasma using high turbulence liquid chromatography online extraction and tandem mass spectrometry
AU Zeng, Wei; Musson, Donald G.; Fisher, Alison L.; Wang, Amy Qiu
CS Department of Drug Metabolism, Merck Research Laboratories, Merck and Co. Inc., West Point, PA, 19486-0004, USA
SO Rapid Communications in Mass Spectrometry (2006), 20(8), 1169-1175
CODEN: RCMSEF; ISSN: 0951-4198
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB A robust and sensitive method using high turbulence liquid chromatog. (HTLC) online extraction with tandem mass spectrometry (MS/MS) for the determination of MK-0431 in human plasma was developed and validated to support the clin. studies. This HTLC online extraction method eliminated the time-consuming off-line sample extraction procedures and significantly increased productivity. A narrow bore large particle size reversed-phase column (Cyclone, 50 × 1.0 mm, 60 μm) and a BDS Hypersil C18 column (30 × 2.1 mm, 3 μm) were used as extraction and anal. columns, resp. The linear dynamic range of the calibration curve was 0.5 to 1000 ng/mL. Intraday validation was conducted using five calibration curves prepared in five lots of human control plasma, and the intraday precision (RSD%) was from 2.4 to 9.0% and the accuracy was from 98.0 to 103% of the nominal value. The intraday precision (RSD%, n = 5) for plasma quality control (QC) samples varied from 2.0 to 5.3% and accuracy from 103 to 105% of the nominal value. The interday precision (RSD%) for 100 sets of plasma QC samples in 29 anal. runs varied from 6.3 to 9.0% and the accuracy from 98.8 to 104% of the nominal value. No significant

difference was observed between the interday and intraday precision and accuracy of the QC samples.
IT 654671-78-0, MK-0431
RL: ANT (Analyte); ANST (Analytical study)
(determination of MK-0431 in human plasma using high turbulence liquid chromatog.
online extraction and tandem mass spectrometry)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

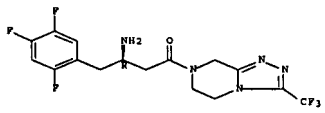
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 72 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:364868 CAPLUS Full-text
DN 144:382039
TI Combination of a DPP-IV inhibitor and a PDGF kinase inhibitor
IN Burkey, Bryan; Hughes, Thomas Edward
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006041976	A1	20060420	WO 2005-US35917	20051006
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2005294320	A1	20060420	AU 2005-294320	20051006
	CA 2580266	A1	20060420	CA 2005-2580266	20051006
	EP 1802308	A1	20070704	EP 2005-801149	20051006
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI	US 2004-617201P	P	20041008		
	WO 2005-US35917	W	20051006		

AB The present invention relates to a combination, such as a combined preparation or pharmaceutical composition, resp., comprising (i) dipeptidyl peptidase (DPP) IV inhibitor or a pharmaceutically acceptable salt thereof, and (ii) at least one PDGF receptor tyrosine kinase inhibitor or a pharmaceutically acceptable salt thereof. The present invention furthermore relates to the use of such a combination for the prevention, delay of progression or treatment of a disease or condition selected from insulin resistance, impaired glucose metabolism (IGT), conditions of impaired glucose tolerance, conditions of impaired fasting plasma glucose, diabetes particularly type 1 or type 2 diabetes mellitus, obesity, diabetic retinopathy, macular degeneration, cataracts, diabetic nephropathy, glomerulosclerosis, diabetic neuropathy, erectile dysfunction, premenstrual syndrome, coronary heart disease, hypertension, angina pectoris, myocardial infarction, stroke, vascular restenosis, skin and connective tissue disorders, foot ulcerations and ulcerative colitis, endothelial dysfunction and impaired vascular compliance, and vascular events, cardiovascular morbidity or mortality associated with diabetes (e.g. type I or II) or IGT. For example, a combination comprises a PDGF receptor kinase inhibitor, i.e., [4-(4-methylpiperazin-1-yl-methyl)-N-[4-methyl-3-(4-pyridin-3-yl)pyrimidin- 2-yl-amino]phenyl]benzamide or 4-methyl-N-[3-(4-methylimidazol-1-yl)-5- trifluoromethylphenyl]-3-(4-pyridin-3-yl-pyrimidin-2-yl-amino)benzamide (50, 100, 200, 300 or 400 mg) or a pharmaceutically acceptable salt thereof, and a DPP-IV inhibitor (S)-1-[(3-hydroxy-1-adamantyl)amino]acetyl- 2-cyanopyrrolidine (50, 100 or 150 mg) or a pharmaceutically acceptable salt thereof.
IT 486460-32-6, Sitagliptin 654671-78-0, MK-0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic uses of combination of DPP-IV inhibitor and PDGF kinase inhibitor)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

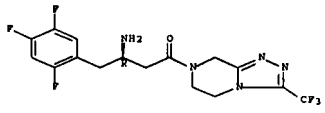


RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

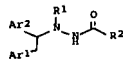
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 73 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:361238 CAPLUS Full-text
DN 144:412373
TI Acyclic hydrazides as cannabinoid receptor modulators
IN Lin, Linus S.; Liu, Ping
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 65 pp.

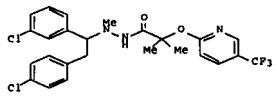
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006041797	A2	20060420	WO 2005-US35560	20051003
WO 2006041797	A3	20060706		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005294506	A1	20060420	AU 2005-294506	20051003
CA 2582588	A1	20060420	CA 2005-2582588	20051003
EP 1807388	A2	20070718	EP 2005-800281	20051003
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2004-616696P	P	20041007		
WO 2005-US35560	W	20051003		

OS CASREACT 144:412373; MARPAT 144:412373
GI



I



II

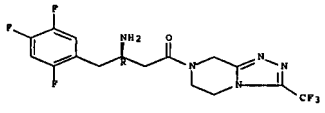
AB The acyclic hydrazides I [R1 = H, C1-4-alkyl, C3-6-cycloalkly, C2-4-alkenyl, C2-4-alkynyl; R2 = C1-10-alkyl, C2-10-alkenyl, C2-10-alkynyl, C3-10-cycloalkyl, (C3-10-cycloalkyl)-(C1-4-alkyl), cycloheteroalkyl, cycloheteroalkyl-(C1-4-alkyl), aryl, aryl-(C1-10-alkyl), aryl-(C2-8-alkenyl), diaryl-(C1-4-alkyl), heteroaryl, heteroaryl-(C1-10- alkyl), NRcRd; Ar1, Ar2 = aryl, heteroaryl; Rc, Rd = H, C1-10-alkyl, C2-10-alkenyl, cycloalkyl, cycloalkyl-(C1-10-alkyl), aryl, heteroaryl, pyridyl, pyrimidinyl, aryl-(C1-10-alkyl), heteroaryl-(C1-10-alkyl); NRcRd = 4- to 7-membered heterocyclic ring

containing 0 - 2 addnl. heteroatoms selected from N, O, S] of the invention are antagonists and/or inverse agonists of the Cannabinoid-1 (CB1) receptor and are useful in the treatment, prevention and suppression of diseases mediated by the CB1 receptor. Thus, hydrazide II was prepared from 3-ClC6H4CHO via imination with MeNH2, Grignard reaction with 4-ClC6H4CH2MgCl, nitrosation with NaNO3 in CH2Cl2 containing N-chlorosuccinimide and PhCH2EC3N+Cl-, reduction with TiCl4/Mg in Et2O, and acylation with 2-methyl-2-[5-(trifluoromethyl)-2- pyridinyloxy]propionic acid. The compds. of the present invention are useful as centrally acting drugs in the treatment of psychosis, memory deficits, cognitive disorders, migraine, neuropathy, neuro-inflammatory disorders including multiple sclerosis and Guillain-Barre syndrome and the inflammatory sequelae of viral encephalitis, cerebral vascular accidents, and head trauma, anxiety disorders, stress, epilepsy, Parkinson's disease, movement disorders, and schizophrenia. The compds. are also useful for the treatment of substance abuse disorders (including smoking cessation), the treatment of obesity or eating disorders, as well as the treatment of asthma, constipation, chronic intestinal pseudo-obstruction, and cirrhosis of the liver. Thus, I were tested for binding to cannabinoid receptor-1 [IC50 = 2μM].

IT 486460-32-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination chemotherapy co-drug; hydrazides as cannabinoid receptor modulators)

RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 74 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:298857 CAPLUS Full-text
DN 144:338150
TI Amorphous form of a phosphoric acid salt of a dipeptidyl peptidase-IV inhibitor
IN Ferlita, Russell R.; Wenslow, Robert M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006033848	A1	20060330	WO 2005-US32079	20050909
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1796671	A1	20070620	EP 2005-796471	20050909
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI US 2004-610019P	P	20040915		
WO 2005-US32079	W	20050909		

AB The present invention relates to a novel amorphous form of the dihydrogenphosphate salt of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine as well as a process for its preparation, pharmaceutical compns. containing this novel form, and methods of use of the novel form and pharmaceutical compns. for the treatment of diabetes, obesity, and high blood pressure.

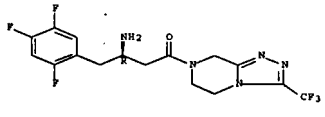
IT 654671-78-0P
RL: PAC (Pharmacological activity); PNU (Preparation, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amorphous form of a phosphoric acid salt of a dipeptidyl peptidase-IV inhibitor)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

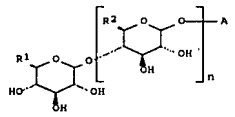
CRN 7664-38-2
CMF H3 O4 P

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

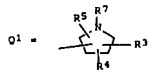
L11 ANSWER 75 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:101593 CAPLUS Full-text
DN 144:171188
TI Preparation of glucopyranosyl-glucopyranosides and related compounds as α-amylase inhibitors
IN Izumi, Masanori; Okuno, Akira; Matsumura, Keiko
PA Sankyo Company, Limited, Japan
SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
PAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006011588	A1	20060202	WO 2005-JP13912	20050729
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CA 2575521	A1	20060202	CA 2005-2575521	20050729
JP 2006063074	A	20060309	JP 2005-219763	20050729
EP 1792620	A1	20070606	EP 2005-767081	20050729
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
PRAI JP 2004-222419	A	20040729		
WO 2005-JP13912	W	20050729		

OS MARPAT 144:171188
GI



I

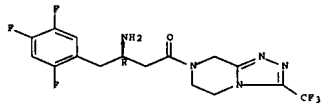


AB The present invention provided the preparation of compds. I [A = Q1, etc.; R1, R2 = alkyl, hydroxymethyl, alkoxymethyl, etc.; R3, R4, R5 = alkyl, alkoxy, hydroxyalkyl, etc.; R7 = alkyl, alkoxy, hydroxyalkyl, etc.; n = 1, 2] and medicaments with at least one drug selected from insulin sensitivity enhancers, insulin secretion accelerators, biguanides, insulin pharmaceuticals, and DPP-IV inhibitors. For example, (2R,3R,4R)-4-hydroxy- 2-(hydroxymethyl)pyrrolidin-3-yl 4-O-(6-deoxy-α-D-glucopyranosyl)- α-D-glucopyranoside (II) was prepared from D-maltose monohydrate in a multistep process. In α-amylase inhibition assays, compound II exhibited the IC50 value of 0.7 μg/mL. Compds. I are claimed useful for the treatment of diabetes.
IT 654671-78-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(medicaments with; preparation of glucopyranosyl-glucopyranosides and related compds. as α-amylase inhibitors for treatment of diabetes)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

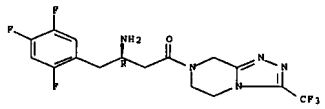
L11 ANSWER 76 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:82491 CAPLUS Full-text
DN 145:1093
TI Glucagon-like peptide-1-based therapies for the treatment of type 2 diabetes mellitus
AU Gallwitz, Baptist
CS Department of Medicine, Eberhard-Karls-University, Tuebingen, Germany
SO Treatments in Endocrinology (2005), 4(6), 361-370
CODEN: TERNAN; ISSN: 1175-6349
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A review. The 'incretin effect' describes the phenomenon of an enhanced insulin response following oral ingestion of glucose compared with that after i.v. administration of glucose, leading to identical postprandial plasma glucose excursions. It accounts for up to 60% of the postprandial insulin secretion, but is diminished in patients with type 2 diabetes mellitus. Gastrointestinal hormones that promote the incretin effect are called incretins. Glucagon-like peptide-1 (GLP-1) is an important incretin. Under hyperglycemic conditions in humans, it stimulates insulin secretion and normalizes blood glucose levels. GLP-1 does not stimulate insulin secretion at normal glucose levels; therefore, it does not cause hypoglycemia. Furthermore, it inhibits glucagon secretion and delays gastric emptying. In vitro and animal data have demonstrated that GLP-1 increases β-cell mass by stimulating islet cell neogenesis and by inhibiting the apoptosis of islet cells. The improvement of β-cell function due to GLP-1 can be indirectly observed from the increased insulin secretory capacity of humans receiving such treatment. GLP-1 may represent an attractive therapeutic method for patients with type 2 diabetes because of its multiple effects, including the simulation of satiety in the CNS by acting as a transmitter or by crossing the blood brain barrier. Native GLP-1 is degraded rapidly upon i.v. or s.c. administration and is therefore not feasible for routine therapy. Long-acting GLP-1 analogs (e.g. liraglutide) and exendin-4 (exenatide) that are resistant to degradation, called 'incretin mimetics', are being investigated in clin. trials. Dipeptidyl peptidase-IV inhibitors (e.g. vildagliptin, sitagliptin, and saxagliptin) that inhibit the enzyme responsible for incretin degradation are also being studied.
IT 654671-78-0, Sitagliptin
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase-IV inhibitor sitagliptin that inhibit enzyme responsible for incretin degradation may prove useful therapeutic option

for treatment of type 2 diabetes mellitus in patient)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

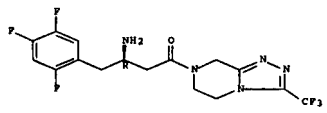
L11 ANSWER 77 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:64377 CAPLUS Full-text
DN 144:323953
TI DPP-4 inhibitor: MK-0431
AU Hojo, Minoru
CS Clinical Development Institute, Banyu Pharmaceutical Co., Ltd., Japan
SO BIO Clinica (2006), 21(1), 73-76
CODEN: BCILCY; ISSN: 0919-8237
PB Hokuryukan
DT Journal; General Review
LA Japanese
AB A review, discussing the action mechanism and clin. pharmacol. of the DPP-4 inhibitor, MK-0431 for treatment of type-2 diabetes.
IT 654671-78-0, MK-0431
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(action mechanism and clin. pharmacol. of the DPP-4 inhibitor, MK-0431

for treatment of type-2 diabetes)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 78 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2006:53972 CAPLUS Full-text
DN 144:121856
TI Combination of dipeptidyl peptidase IV (DPP-IV) inhibitors and compounds modulating 5-HT3 and/or 5-HT4 receptors for therapeutic use
IN Villhauer, Edwin Bernard
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2006005613	A1	20060119	WO 2005-EP7636	20050713

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,

NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

AU 2005261778	A1	20060119	AU 2005-261778	20050713
CA 2573209	A1	20060119	CA 2005-2573209	20050713
EP 1768664	A1	20070404	EP 2005-761596	20050713

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR

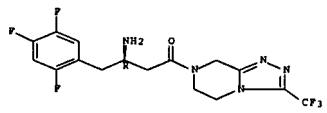
PRAI US 2004-588011P	P	20040714	
WO 2005-EP7636	W	20050713	

AB The invention discloses a combination, such as a combined preparation or pharmaceutical composition, resp., comprising of a DPP-IV inhibitor or a pharmaceutically acceptable salt thereof and comprising at least one therapeutic agent selected from an agent interacting with a 5-HT3 receptor and/or an agent interacting with 5HT4 receptor, or a pharmaceutically acceptable salt thereof. The invention furthermore discloses the use of such a combination for the prevention, delay of progression, or treatment of diseases and disorders selected from selected from insulin resistance, impaired glucose metabolism, conditions of impaired glucose tolerance, conditions of impaired fasting plasma glucose, diabetes particularly type 2 diabetes mellitus, obesity, diabetic retinopathy, macular degeneration, cataracts, diabetic nephropathy, glomerulosclerosis, diabetic neuropathy, erectile dysfunction, premenstrual syndrome, coronary heart disease, hypertension, angina pectoris, myocardial infarction, stroke, vascular restenosis, skin and connective tissue disorders, foot ulceration's and ulcerative colitis, endothelial dysfunction and impaired vascular compliance, altered gastrointestinal motility, sensitivity and/or secretion disorder(s) which include, but are not limited to, heartburn, bloating, postoperative ileus, abdominal pain and discomfort, early satiety, epigastric pain, nausea, vomiting, burbulence, regurgitation, intestinal pseudoobstruction, anal incontinence, GERD, IBS, dyspepsia, chronic constipation or diarrhea, diabetic gastropathy, gastroparesis, e.g. diabetic gastroparesis, ulcerative colitis, Crohn's disease, ulcers and the visceral pain associated therewith.
IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibitor combination with compds. modulating 5-HT3 and/or 5-HT4 receptors for therapeutic use)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

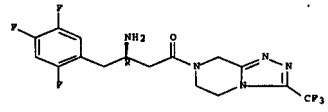
L11 ANSWER 79 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1302281 CAPLUS Full-text
DN 144:425470
TI Pharmacokinetics and pharmacodynamics of sitagliptin, an inhibitor of dipeptidyl peptidase IV, in healthy subjects: Results from two randomized, double-blind, placebo-controlled studies with single oral doses
AU Herman, Gary A.; Stevens, Cathy; Van Dyck, Kristien; Bergman, Arthur; Yi, Bingming; De Smet, Marina; Snyder, Karen; Hilliard, Deborah; Tanen, Michael; Tanaka, Wesley; Wang, Amy Q.; Zeng, Wei; Musson, Donald; Winchell, Gregory; Davies, Michael J.; Ramael, Steven; Gottesdiener, Keith M.; Wagner, John A.
CS Whitehouse Station, and SGS Biopharma, Merck & Co, Antwerp, Belg.
SO Clinical Pharmacology & Therapeutics (New York, NY, United States) (2005), 78(6), 675-688
CODEN: CLPTAT; ISSN: 0009-9236
PB Elsevier
DT Journal
LA English
AB Background: Sitagliptin (MK-0431 [(2R)-4-oxo-4-(3-[trifluoromethyl]-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7[8H]-yl)-1-(2,4,5-trifluorophenyl)butan-2-amine]) is an orally active, potent, and selective inhibitor of dipeptidyl peptidase IV (DPP-IV) currently in phase III development for the treatment of type 2 diabetes. Methods: Two double-blind, randomized, placebo-controlled, alternating-panel studies evaluated the safety, tolerability, pharmacokinetics, and pharmacodynamics of single oral doses of sitagliptin (1.5-600 mg) in healthy male volunteers. Results: Sitagliptin was well absorbed (approx. 80% excreted unchanged in the urine) with an apparent terminal half-life ranging from 8 to 14 h. Renal clearance of sitagliptin averaged 388 mL/min and was largely uninfluenced by the dose administered. The area under the plasma concentration-time curve for

sitagliptin increased in an approx. dose-dependent manner and was not meaningfully influenced by food. Single doses of sitagliptin markedly and dose-dependently inhibited plasma DPP-IV activity, with approx. 80% or greater inhibition of DPP-IV activity occurring at 50 mg or greater over a 12-h period and at 100 mg or greater over a 24-h period. Compared with placebo, sitagliptin produced an approx. 2-fold increase in postmeal active glucagon-like peptide 1 levels. Sitagliptin was well tolerated and was not associated with hypoglycemia. Conclusions: This study provides proof of pharmacol. characteristics for sitagliptin in humans. By inhibiting plasma DPP-IV activity, sitagliptin increases the postprandial rise in active glucagon-like peptide 1 concns. without causing hypoglycemia in normoglycemic healthy male volunteers. Sitagliptin possesses pharmacokinetic and pharmacodynamic characteristics that support a once-daily dosing regimen.
IT 654671-78-0, Sitagliptin
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(single oral dose sitagliptin was well absorbed, tolerated increase plasma postprandial active glucagon-like peptide 1, inhibited dipeptidyl peptidase IV activity and did not cause adverse effect as hypoglycemia in normoglycemic human)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 80 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1290025 CAPLUS Full-text
DN 144:36329
TI Thiazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Cow, Christopher; Xie, Yongping; Wang, Xing; Russo, Ross; Azimioara, Mihai; Saez, Enrique
PA IRM LLC, Bermuda
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005116000	A1	20051208	WO 2005-US18167	20050524
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005247931	A1	20051208	AU 2005-247931	20050524
	CA 2563818	A1	20051208	CA 2005-2563818	20050524
	EP 1748993	A1	20070207	EP 2005-754130	20050524
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1980906	A	20070613	CN 2005-80016538	20050524
	IN 2006CN04307	A	20070615	IN 2006-CN4307	20061123
	NO 2006005984	A	20070205	NO 2006-5984	20061222
PRAI	US 2004-574137P	P	20040524		
	US 2005-648985P	P	20050131		
	WO 2005-US18167	W	20050524		

OS MARPAT 144:36329
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to thiazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, p is 0-3; L is selected from -XOX-, -XS(O)mX-, and -XS(O)mXO-, where m is 0-2 and X is a bond or (un)substituted C1-4 alkylene; R1 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; R2 is -XOXCO2R5 or -XCO2R5, where X is as defined previously and R5 is H or C1-6 alkyl; and R3 and R4 are independently selected from R6 and R6Y, where R6 is (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13

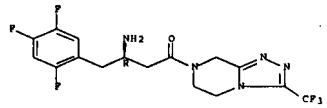
heteroaryl, and Y is selected from C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, -C(O)N(R5)-, and -OX-, where X and R5 are as defined previously, or R3 and R4, together with the atoms to which they are attached, form fused bi- or tricyclic C5-14 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Cyclocondensation of 2-bromo-4'-methoxyacetophenone with thioacetamide followed by bromination, demethylation, and alkylation with iso-Pr iodide gave bromothiazole II, which was brominated and substituted with phenol III (preparation in 3 steps from 4-hydroxy-3-methylacetophenone given) to give thiazole IV. Compound IV underwent Suzuki coupling with 4-(trifluoromethoxy)phenylboronic acid and ester hydrolysis to give thiazole V. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of thiazole compds. as PPAR modulators and their use for treatment and prevention of diseases associated with PPARδ activity)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 81 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1289979 CAPLUS Full-text
DN 144:36326
TI Oxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Xie, Yongping; Wang, Xing; Cow, Christopher; Russo, Ross
PA IRM LLC, Bermuda
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005116016	A1	20051208	WO 2005-US18166	20050524
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005247930	A1	20051208	AU 2005-247930	20050524
	CA 2563819	A1	20051208	CA 2005-2563819	20050524
	EP 1749003	A1	20070207	EP 2005-775612	20050524
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1980919	A	20070613	CN 2005-80016511	20050524
	IN 2006CN04308	A	20070615	IN 2006-CN4308	20061123
	NO 2006005983	A	20070205	NO 2006-5983	20061222
PRAI	US 2004-574137P	P	20040524		
	US 2005-649671P	P	20050202		
	WO 2005-US18166	W	20050524		

OS MARPAT 144:36326
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to oxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, p is 0-3; L is selected from -XOX-, -XS(O)mX-, and -XS(O)mXO-, where m is 0-2 and X is a bond or (un)substituted C1-4 alkylene; R1 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; R2 is -XOXCO2R5 or -XCO2R5, where X is as defined previously and R5 is H or C1-6 alkyl; and R3 and R4 are independently selected from R6 and

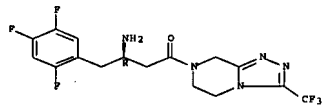
R6Y, where R6 is (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-13 heteroaryl, and Y is selected from C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, -C(O)N(R5)-, and -OX-, where X and R5 are as defined previously, or R3 and R4, together with the atoms to which they are attached, form fused bi- or tricyclic C5-14 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Diazotization of 4-(trifluoromethoxy)acetophenone followed by heterocyclization with acetonitrile, and bromination gave bromooxazole II, which was brominated and substituted with phenol III (preparation in 3 steps from 4-hydroxy-3-methylacetophenone given) to give oxazole IV. Compound IV underwent Suzuki coupling with 2-isopropoxypyridin-5-ylboronic acid (preparation from 2-chloro-5-bromopyridine given) and ester hydrolysis to give oxazole V. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of oxazoles as PPAR modulators and their use for treatment and prevention of diseases associated with PPARδ activity)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 82 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1262399 CAPLUS Full-text
DN 144:22712
TI Triaryl compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Azimioara, Mihai
PA Irm-LLC, Bermuda
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005113506	A1	20051201	WO 2005-US16747	20050513
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005245418	A1	20051201	AU 2005-245418	20050513
	CA 2564365	A1	20051201	CA 2005-2564365	20050513
	EP 1756062	A1	20070228	EP 2005-751010	20050513
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1980894	A	20070613	CN 2005-80019645	20050513
	IN 2006CN04198	A	20070615	IN 2006-CN4198	20061114
PRAI	US 2004-571004P	P	20040514		
	WO 2005-US16747	W	20050513		

OS MARPAT 144:22712
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to aryl compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, m is 0-3; X, Y, and Z are independently selected from CH and N; L is (un)substituted (CH2)nO(CH2)n or (CH2)nS(O)p(CH2)n, where each n is

independently selected from 0-4 and p is 0-2; R1 and R2 are independently selected from (un)substituted C3-12 cycloalkyl-A-, (un)substituted C3-8 heterocyclyl-A-, (un)substituted C6-10 aryl-A-, and (un)substituted C5-13 heteroaryl-A-, where A is a bond, C1-6 alkylene, C2-6 alkenylene, or C2-6 alkynylene; R3 is selected from halo, C1-6 alkyl, C1-6 alkoxy, C1-6 hydroxyalkyl, C1-6 haloalkyl, C1-6 haloalkoxy, (un)substituted C6-10 aryl, (un)substituted C5-10 heteroaryl, (un)substituted C3-12 cycloalkyl, and (un)substituted C3-8 heterocyclyl; and R4 is selected from (CH2)nO(CH2)nCO2R5 and (CH2)nCO2R5, where n is as defined previously and R5 is H or C1-6 alkyl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Substitution of Me bromoacetate with 4-hydroxy-3- methylacetophenone followed by Baeyer-Villiger oxidation and methanolysis gave phenoxyacetate II, which underwent substitution of 3,5-dibromobenzyl bromide to give dibromobenzyl ether III. Treatment of III with an excess of 4-trifluoromethylphenylboronic acid and ester hydrolysis resulted in the formation of terphenyl IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

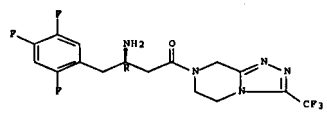
IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of triaryl compds. as PPAR modulators and their use for treatment and prevention of diseases associated with PPARδ activity)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 83 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1259663 CAPLUS Full-text
DN 144:22911
TI Isoxazole compounds as PPAR modulators, their preparation, pharmaceutical compositions, and use in therapy
IN Epple, Robert; Russo, Ross; Azimioara, Mihai; Xie, Yongping
PA IRM LLC, Bermuda
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005113519	A1	20051201	WO 2005-US16672	20050512
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005245411	A1	20051201	AU 2005-245411	20050512
	CA 2564429	A1	20051201	CA 2005-2564429	20050512
	EP 1745027	A1	20070124	EP 2005-769154	20050512
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1984894	A	20070620	CN 2005-80019652	20050512
	IN 2006CN04201	A	20070622	IN 2006-CN4201	20061114
PRAI	US 2004-571003P	P	20040514		
	WO 2005-US16672	W	20050512		

OS MARPAT 144:22911
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to isoxazole compds. of formula I, which are modulators of peroxisome proliferator-activated receptors (PPAR), particularly PPARδ. In compds. I, R1 is selected from (un)substituted C1-6 alkyl, (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl,

and (un)substituted C5-10 heteroaryl; R2 is selected from (CH2)nO(CH2)nOR5, (CH2)nOR5, CO2R5, C(O)N(R4)2, C(O)N(R4)(CH2)nOR4, CO2(CH2)nOR5, C(O)(CH2)nOR5, C(O)N(R4)(CH2)nOR5, C(O)N(R4)(R5), and C(O)N(R4)(CH2)nR5, where n is 0-4, R4 is H or C1-6 alkyl, and R5 is C1-6 alkyl, C3-12 cycloalkyl, C3-8 heterocyclyl, C6-10 aryl, or C5-10 heteroaryl, or R4 and R5, together with the nitrogen atom to which they are attached, form C3-8 heterocyclyl or C5-10 heteroaryl; and R3 is selected from (un)substituted C3-12 cycloalkyl, (un)substituted C3-8 heterocyclyl, (un)substituted C6-10 aryl, and (un)substituted C5-10 heteroaryl; including pharmaceutically acceptable salts, hydrates, solvates, isomers, and prodrugs thereof. The invention also relates to the preparation of I, pharmaceutical compns. comprising a therapeutically effective amount of compound I in combination with one or more pharmaceutically acceptable excipients, as well as to the use of the compns. to treat or prevent diseases or disorders associated with PPAR activity. Esterification of 3-bromophenylacetic acid followed by coupling with cyanide, reduction of the nitrile to an aldehyde, condensation with hydroxylamine, and chlorination gave chlorooxime II. N-Boc-2-bromoethylamine was substituted with 2,4-dichlorophenol followed by deprotection, amidation with Et benzoylacetate to give benzoylacetamide III, which underwent cyclocondensation with chlorooxime II and ester hydrolysis, resulting in the formation of isoxazole IV. Most preferred compds. of the invention express an EC50 value for PPARδ of less than 100 nM. The compds. of the invention are at least 100-fold selective for PPARδ over PPARγ.

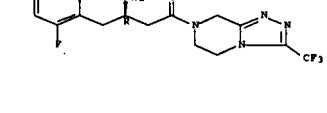
IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compds. and compns. as PPAR modulators and their use for treatment and prevention of diseases associated with activity of PPAR families, particularly PPARδ)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

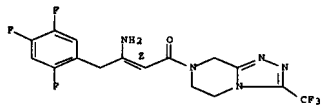
L11 ANSWER 84 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1123877 CAPLUS Full-text
DN 143:387377
TI Process for the preparation of enantiomerically enriched β-amino acid derivatives
IN Xiao, Yi; Sun, Yongkui; Rosner, Thorsten; Rivera, Nelo R.; Krska, Shane W.; Clausen, Andrew M.; Armstrong, Joseph D., III; Spindler, Felix; Malan, Christophe
PA Merck & Co., Inc., USA; Solvias A.-G.
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005097733	A1	20051020	WO 2005-US11585	20050405
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2005230693	A1	20051020	AU 2005-230693	20050405
CA 2561973	A1	20051020	CA 2005-2561973	20050405
EP 1735269	A1	20061227	EP 2005-732844	20050405
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR			
CN 1972898	A	20070530	CN 2005-80010669	20050405
IN 2006CN03581	A	20070622	IN 2006-CN3581	20060928
PRAI US 2004-559514P	P	20040405		
US 2005-646698P	P	20050124		
WO 2005-US11585	W	20050405		

OS CASREACT 143:387377; MARPAT 143:387377
AB Enantiomerically-enriched β-amino acid derivs. having unprotected amino group were prepared by enantioselective hydrogenation of an amine-unprotected prochiral β-amino acrylic acid or derivative in the presence of a rhodium metal precursor complexed with a chiral mono- or bisphosphine ligand. The product chiral β-amino acid derivs. are useful in the asym. synthesis of biol. active mols. Thus, hydrogenation of H2NCPh:CHCO2Me in the presence of [Rh(cod)Cl]2 and a ferrocenyl bisphosphine ligand afforded 92% H2NCHPhCH2CO2Me.

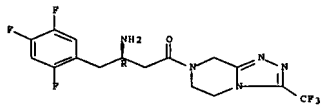
IT 767340-03-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of enantiomerically-enriched β-amino acid derivs. by catalytic hydrogenation of β-amino acrylic acids)
RN 767340-03-4 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(2Z)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)-2-butenyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 486460-32-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of enantiomerically-enriched β-amino acid derivs. by catalytic hydrogenation of β-amino acrylic acids)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

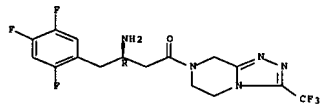


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 85 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1080535 CAPLUS Full-text
DN 143:432008
TI Structure-Based Virtual Screening for Low Molecular Weight Chemical Starting Points for Dipeptidyl Peptidase IV Inhibitors
AU Ward, Richard A.; Perkins, Tim D. J.; Stafford, Jackie
CS Cancer Discovery, AstraZeneca, Macclesfield /Cheshire, SK10 4TG, UK
SO Journal of Medicinal Chemistry (2005), 48(22), 6991-6996
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal

LA English
AB Structure-based virtual screening was performed against the target dipeptidyl peptidase IV (DPP-IV) to identify good chemical starting points for medicinal chemical A database of available compds. was filtered by calculated phys. properties and undesired chemical This database was matched against two inhouse designed DPP-IV pharmacophores, and the hits from these pharmacophore searches were docked into a DPP-IV crystal structure. Compds. were then selected for testing and 51 active compds. were identified from a list of 4000 compds. tested. These had activities ranging from 30% to 82% when tested at a concentration of 30 μM in an enzyme inhibition assay.
IT 486460-32-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-based screening for low mol. weight chemical starting points for dipeptidyl peptidase IV inhibitors)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 86 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:1050865 CAPLUS Full-text
DN 143:347172
TI Preparation of imidazoles as inhibitors of glutaminyl cyclase.
IN Schilling, Stephan; Buchholz, Mirko; Niestroj, Andre Johannes; Heiser, Ulrich; Demuth, Hans-Ulrich
PA Probiodrug AG, Germany
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 838,993.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2005215573	A1	20050929	US 2005-51760	20050204
US 2004224875	A1	20041111	US 2004-838993	20040505
PRAI US 2004-542133P	P	20040205		
US 2004-838993	A2	20040505		
US 2004-634364P	P	20041208		
US 2003-468014P	P	20030505		

OS CASREACT 143:347172; MARPAT 143:347172
GI

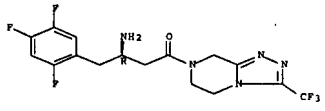
I

AB Title compds. [I; A = (Ph-, cycloalkyl-interrupted) alkylene, alkenylene, alkynylene; B = NHC(:X)NHD, C(:X)NHD, C(:X)SD, etc.; D = alkyl, alkenyl, alkynyl, cycloalkyl, aryl, acyl, heterocyclyl, etc.; X = O, S, imino, (substituted) CH2], with specific exceptions, were prepared Thus, 3,4-methylenedioxyphenyl isothiocyanate and 3-(1H-imidazol-1- yl)propylamine were refluxed together for 2 h in EtOH to give 51.3% 1-[3-(1H-imidazol-1-yl)propyl]-3-(3,4-dimethoxyphenyl)thiourea. The latter showed an IC50 = 0.22 μM for inhibition of glutaminyl cyclase. Peptide inhibitors of dipeptidyl peptidase IV were also prepared
IT 654671-78-0, MK431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy; preparation of imidazoles as inhibitors of glutaminyl cyclase)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 87 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:962041 CAPLUS Full-text
DN 143:242034
TI DPP-IV inhibitors for neurodegenerative and cognitive disorders
IN Hughes, Thomas Edward
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

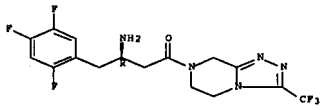
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005079795	A2	20050901	WO 2005-EP1729	20050218
	WO 2005079795	A3	20051110		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005215136	A1	20050901	AU 2005-215136	20050218
	CA 2555399	A1	20050901	CA 2005-2555399	20050218
	EP 1732550	A2	20061220	EP 2005-707520	20050218
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	CN 1921856	A	20070228	CN 2005-80005568	20050218
	BR 2005007905	A	20070710	BR 2005-7905	20050218
	IN 2006CN03029	A	20070608	IN 2006-CN3029	20060818
PRAI	US 2004-546229P	P	20040220		
	US 2004-607902P	P	20040908		
	WO 2005-EP1729	W	20050218		

AB The invention relates to the use of a dipeptidyl peptidase IV inhibitor (DPP-IV inhibitor) or a pharmaceutically acceptable salt thereof for the prevention, delay of progression or the treatment of neurodegenerative disorders, cognitive disorders and for improving memory (both short term and long term) and learning ability.
IT 654671-78-0, MK-0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DPP-IV inhibitors for neurodegenerative and cognitive disorders)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

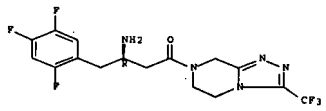
L11 ANSWER 88 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:945302 CAPLUS Full-text
DN 143:422325
TI First Generation Process for the Preparation of the DPP-IV Inhibitor Sitagliptin
AU Hansen, Karl B.; Balsells, Jaume; Dreher, Spencer; Hsiao, Yi; Kubryk, Michele; Palucki, Michael; Rivera, Nelo; Steinhuebel, Dietrich; Armstrong, Joseph D., III; Askin, David; Grabowski, Edward J. J.
CS Department of Process Research, Merck Research Laboratories, Rahway, NJ, 07065, USA
SO Organic Process Research & Development (2005), 9(5), 634-639
CODEN: OPRDFK; ISSN: 1083-6160
PB American Chemical Society
DT Journal
LA English
OS CASREACT 143:422325
AB A new synthesis of sitagliptin (MK-0431), a DPP-IV inhibitor and potential new treatment for type II diabetes, suitable for the preparation of multi-kilogram quantities is presented. The triazolopyrazine fragment of sitagliptin was prepared in 26% yield over four chemical steps using a synthetic strategy similar to the medicinal chemical synthesis. Key process developments were made in the first step of this sequence, the addition of hydrazine to chloropyrazine, to ensure its safe operation on a large scale. The beta-amino acid fragment of sitagliptin was prepared by asym. reduction of the corresponding beta-ketoester followed by a two-step elaboration to an N-benzyloxy beta-lactam. Hydrolysis of the lactam followed by direct coupling to the triazolopiperazine afforded sitagliptin after cleavage of the N-benzyloxy group and salt formation. The overall yield was 52% over eight steps.
IT 654671-78-0P, Sitagliptin
RL: SPN (Synthetic preparation); PREP (Preparation)
(first generation process for preparation of DPP-IV inhibitor sitagliptin)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.

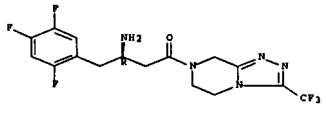


CM 2

CRN 7664-38-2
CMF H3 O4 P

IT 486460-32-6P, (2R)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(first generation process for preparation of DPP-IV inhibitor sitagliptin using free base as synthetic intermediate)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

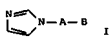


RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

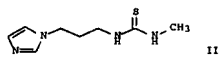
L11 ANSWER 89 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:823672 CAPLUS Full-text
DN 143:229851
TI Preparation of imidazolyl thiourea derivatives as inhibitors of glutaminyl cyclase
IN Schilling, Stephan; Buchholz, Mirko; Niestroj, Andre Johannes; Demuth, Hans-Ulrich; Heiser, Ulrich
PA Probiodrug A.-G., Germany
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005075436	A2	20050818	WO 2005-EP1153	20050204
	WO 2005075436	A3	20051208		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004224875	A1	20041111	US 2004-838993	20040505
	AU 2005210004	A1	20050818	AU 2005-210004	20050204
	CA 2554809	A1	20050818	CA 2005-2554809	20050204
	EP 1713780	A2	20061025	EP 2005-707206	20050204
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
	CN 1918131	A	20070221	CN 2005-80004289	20050204
	BR 2005007485	A	20070710	BR 2005-7485	20050204
	JP 2007520520	T	20070726	JP 2006-551809	20050204
	IN 2006KN02139	A	20070518	IN 2006-KN2139	20060728
	MX 2006PA08868	A	20061030	MX 2006-PA8868	20060804
PRAI	US 2004-542133P	P	20040205		
	US 2004-838993	A	20040505		
	US 2004-634364P	P	20041208		
	US 2003-468014P	P	20030505		
	WO 2005-EP1153	W	20050204		

OS MARPAT 143:229851
GI



I



II

AB Title compds. I [A = alkyl, alkenyl, alkynyl, etc.; B = substituted thiourea, urea, amide, etc.] and their pharmaceutical acceptable salts, are prepared and disclosed as glutaminyl cyclase inhibitors. Thus, e.g., II was prepared by coupling of 1H-imidazole-1-propanamine with the corresponding isothiocyanate. The inhibitory activity of I towards DP IV was evaluated using chromogenic enzyme assay and it was revealed that selected compds. of the invention displayed Ki values in the range of 0.06 up to 204.5 μM. I as glutaminyl cyclase inhibitors should prove useful in the treatment of Alzheimer's disease, depression and dementia. Pharmaceutical compns. comprising I are disclosed.

IT 654671-78-0, MK-431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drugs; preparation of imidazolyl thiourea derivs. as inhibitors of glutaminyl cyclase)

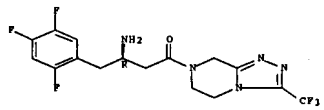
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 90 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:729507 CAPLUS Full-text

DN 143:216652

TI Novel crystalline salts of a dipeptidyl peptidase-IV inhibitor

IN Ferlita, Russell R.; Hansen, Karl; Vydra, Vicky K.; Wang, Yaling; Lindemann, Christopher M.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005072530	A1	20050811	WO 2005-US951	20050112
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, SC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1708571	A1	20061011	EP 2005-705553	20050112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
PRAI US 2004-537073P	P	20040116		
WO 2005-US951	W	20050112		

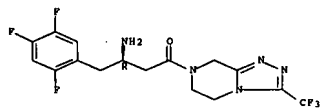
AB Novel crystalline salts of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine (I) are potent inhibitors of dipeptidyl peptidase-IV and are useful for the treatment of non-insulin dependent (type 2) diabetes mellitus. The invention also relates to pharmaceutical compns. containing these novel salts, processes to prepare these salts and their pharmaceutical compns. as well as uses thereof for the treatment of type 2 diabetes. The procedure for preparing I is given.

IT 486460-32-6P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(crystalline salts of dipeptidyl peptidase-IV inhibitor)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 862156-86-3P 862156-87-4P 862156-90-9P
862156-92-1P 862156-93-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline salts of dipeptidyl peptidase-IV inhibitor)

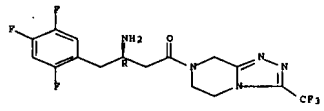
RN 862156-86-3 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monobenzenesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 98-11-3
CMF C6 H6 O3 S

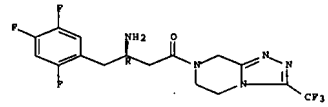
RN 862156-87-4 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, mono(4-methylbenzenesulfonate) (9CI) (CA INDEX NAME)

CM 1

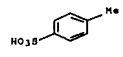
CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



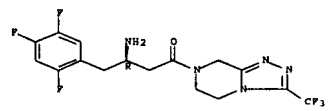
RN 862156-90-9 CAPLUS

CN Bicyclo[2.2.1]heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-, (1R,4R)-, compd. with 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

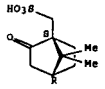
Absolute stereochemistry.



CM 2

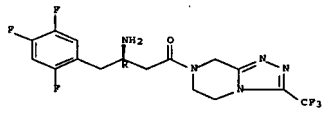
CRN 3144-16-9
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (+).



RN 862156-92-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monohydrochloride, monohydrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

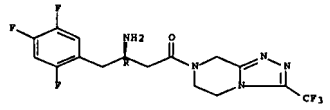
● H_2O

RN 862156-93-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (2R,3R)-2,3-dihydroxybutanedioate, hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

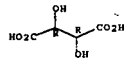
Absolute stereochemistry.



CM 2

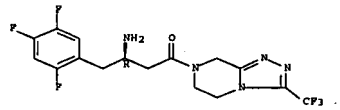
CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



IT 486459-71-6 862156-85-2 862156-88-5
962156-89-6 862156-91-0
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystalline salts of dipeptidyl peptidase-IV inhibitor)
RN 486459-71-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



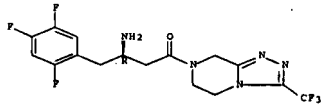
● HCl

RN 862156-85-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

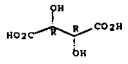
Absolute stereochemistry.



CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

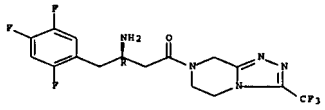


RN 862156-88-5 CAPLUS
CN Bicyclo[2.2.1]heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-, compd. with 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

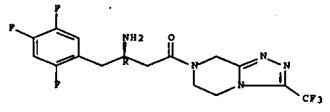
CRN 5872-08-2
CMF C10 H16 O4 S

RN 862156-89-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (2S,3S)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

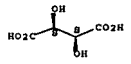
Absolute stereochemistry.



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

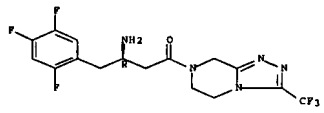


RN 862156-91-0 CAPLUS
CN Bicyclo[2.2.1]heptane-1-methanesulfonic acid, 7,7-dimethyl-2-oxo-, (1R,4S)-, compd. with 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

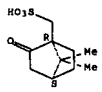
Absolute stereochemistry.



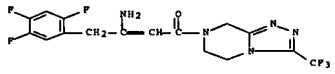
CM 2

CRN 35963-20-3
CMF C10 H16 O4 S

Absolute stereochemistry. Rotation (-).



IT 847445-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystalline salts of dipeptidyl peptidase-IV inhibitor)
RN 847445-81-2 CAPLUS
CN 2-Buten-1-one, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)- (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 91 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2005:696517 CAPLUS Full-text
DN 143:186770
TI Glutaminyl cyclase inhibitors optionally combined with other agents for the treatment of neuronal disorders
IN Schulz, Ingo; Schilling, Stephan; Niestroj, Andre Johannes; Heiser, Ulrich; Demuth, Hans-Ulrich; Rossner, Steffen
PA Probiodrug AG, Germany
SO U.S. Pat. Appl. Publ., 70 pp., Cont.-in-part of U.S. Ser. No. 976,677.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

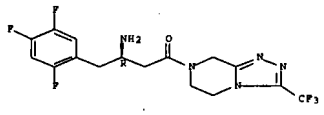
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005171112	A1	20050804	US 2004-2169	20041202
	US 2005137142	A1	20050623	US 2004-976677	20041029
	US 2006100253	A1	20060511	US 2005-290735	20051130
	WO 2006058720	A2	20060608	WO 2005-EP12765	20051130
	WO 2006058720	A3	20060727		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRAI	US 2003-516717P	P	20031103		
	US 2004-976677	A2	20041029		
	US 2004-2169	A2	20041202		
	US 2005-684137P	P	20050524		

OS MARPAT 143:186770
AB The invention provides a method for the treatment of neuronal disorders in a mammal, e.g. a human, which comprises administering an effective, nontoxic and pharmaceutically acceptable amount of at least one glutaminyl cyclase inhibitor, optionally in combination with at least one agent selected prolyl endopeptidase inhibitors, LiCl, inhibitors of dipeptidyl peptidase IV/DP IV-like enzymes, NPY-receptor ligands, NPY agonists, NPY antagonists, acetylcholinesterase inhibitors, protein isoaspartate carboxymethyl transferase enhancers, inhibitors of β-secretases, inhibitors of γ-secretases and inhibitors of neutral endopeptidase, to a mammal in need thereof.
IT 654671-78-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glutaminyl cyclase inhibitors optionally combined with other agents for treatment of neuronal disorders)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



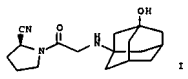
CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 92 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:673144 CAPLUS Full-text
DN 143:179590
TI Direct compression formulation for dipeptidylpeptidase IV inhibitors
IN Kowalski, James; Parthiban, Lakshman Jayanth; Patel, Arun P.
PA Novartis AG, Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005067976	A2	20050728	WO 2005-EP400	20050117
	WO 2005067976	A3	20061116		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005205055	A1	20050728	AU 2005-205055	20050117
	CA 2552569	A1	20050728	CA 2005-2552569	20050117
	EP 1715893	A2	20061102	EP 2005-700976	20050117
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
	BR 2005007007	A	20070605	BR 2005-7007	20050117
	JP 2007518760	T	20070712	JP 2006-549999	20050117
	MX 2006PA08265	A	20060831	MX 2006-PA8265	20060720
	IN 2006CN02669	A	20070608	IN 2006-CN2669	20060720
	NO 2006003739	A	20061020	NO 2006-3739	20060821
PRAI	US 2004-537706P	P	20040120		
	US 2004-604274P	P	20040825		
	WO 2005-EP400	W	20050117		

GI



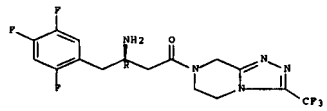
I

AB Dipeptidylpeptidase IV inhibitor (referred to as DPP-IV) that may be 98.5-100% pure is a high-dose drug capable of being directly compressed with specific excipients into solid form dosage forms, such as tablets and capsules having desired, hardness, disintegrating ability and acceptable dissoln. characteristics. DPP-IV is not inherently compressible and thus presents formulation problems. Excipients used in the formulation enhance the flow and compaction properties of the drug and tableting mix. Optimal flow contributes to uniform die fill and weight control. The binder used ensures sufficient cohesive properties that allow DPP-IV to be compressed using the direct compression method. The tablets produced provide an acceptable in vitro dissoln. profile. A composition contained LAF 237 (I), cellulose, lactose, Na starch glycolate, and Mg stearate.
IT 654671-78-0, MK-0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(direct compression formulation for dipeptidylpeptidase IV inhibitors)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

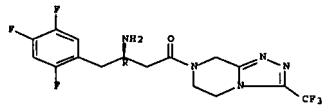
L11 ANSWER 93 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:571490 CAPLUS Full-text
DN 144:192453
TI MK-0431 : agent for type 2 diabetes and dipeptidyl-peptidase IV (CD26) inhibitor
AU Sorbera, L. A.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (2005), 30(4), 337-343
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
AB A review. The incretin hormone glucagon-like peptide-1 (GLP-1, GLP-1[7-36]amide) plays a crucial role in the regulation of insulin by acting on the pancreas to potentiate glucose-induced insulin secretion. GLP-1 also beneficially slows gastric emptying, reduces appetite and restores β-cell function, and has been the subject of research efforts to develop agents for the treatment of type 2 diabetes. However, GLP-1 has an extremely short half-life and is not suitable for therapeutic use. It is rapidly hydrolyzed by the circulating enzyme dipeptidyl-peptidase IV (DPP-IV), which cleaves the mol. at the N-terminal, giving rise to the inactive truncated fragment GLP-1(9-36)amide. On the other hand, administration of a DPP-IV inhibitor could enhance the half-life of GLP-1 and could therefore produce the same pleiotropic effects as exogenously administered GLP-1 or GLP-1 analogs. Thus, one of the newer targets for the treatment of diabetes is the serine protease DPP-IV. MK-0431 (Ono-5435) is a novel, potent, orally active β-amino acid-derived DPP-IV inhibitor that has exhibited good pharmacokinetics in mice, rats, dogs and monkeys and was chosen for further development as a treatment for type 2 diabetes. It has been shown to be effective in insulin-resistant mice and mice with diet-induced obesity, and was safe and effective in patients with type 2 diabetes. The agent has reached phase III development as a treatment for this condition.

IT 654671-78-0P, MK 0431
RL: PAC (Pharmacological activity); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(chemical, pharmacol., pharmacokinetics, and clin. studies of MK-0431 as agent for type 2 diabetes and dipeptidyl-peptidase IV inhibitor)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 94 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:493507 CAPLUS Full-text
DN 143:43869
TI Preparation of nitrogen containing bicyclic pyridine-based derivatives as inhibitors of HMG CoA reductase
IN O'Connor, Stephen P.; Robl, Jeffrey; Ahmad, Saleem; Bisaha, Sharon; Murugesan, Natesan; Ngu, Khehyong; Shi, Yan; Stein, Philip D.; Soundararajan, Nachimuthu; Natalie, Kenneth J., Jr.; Kolla, Laxma R.; Sausker, Justin; Quinlan, Sandra L.; Fan, Junying; Petsch, Dejah; Guo, Zhenrong
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 193 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005051386	A1	20050609	WO 2004-US39051	20041119
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2005171140	A1	20050804	US 2004-989138	20041115
	EP 1684754	A1	20060802	EP 2004-811719	20041119
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				
PRAI	US 2003-523546P	P	20031120		
	US 2004-989138	A	20041115		
	WO 2004-US39051	W	20041119		

OS MARPAT 143:43869
GI

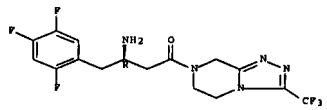
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Het = 5- to 8-membered ring including at least one nitrogen atom with provisions; n = 0-1; R1 and R2 independently = H, alkyl, alkenyl, etc.; R3 = H, aryl, cycloalkyl, etc.; R4 and R5 independently = H, alkyl; X = -CR6R7-CR6aR7a-, -CR6=CR7-; R6, R7, R6a and R7a independently = H, alkyl] and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of HMG CoA reductase. Thus, e.g., II was prepared by cyclization of Et 2-amino-4-(4-fluorophenyl)-6-isopropyl- 5-methoxycarbonyl-3-pyridinepropanoate (preparation given) followed by a reduction/sulfonylation/reduction sequence to give [4-(4-fluorophenyl)-2-isopropyl- 8-methanesulfonyl-5,6,7,8-tetrahydro[1,8]naphthyridin-3-yl]-methanol (III). III was oxidized to the resp. aldehyde and coupled with 1,1-dimethylethyl(4R,6S)-2,2-dimethyl-6-(1-phenyl-1H-tetrazole-5- sulfonylmethyl)-[1,3]dioxan-4-yl-acetate followed by ring opening to give II. I should display activity as inhibitors of HMG CoA reductase (no data given). I as inhibitors of HMG CoA reductase inhibitors should prove useful in the treatment of, but not limited to, hyperlipidemia, dyslipidemia, and atherosclerosis. Pharmaceutical compns. comprising I are disclosed.
IT 654671-78-0, MK 431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(claimed co-drug; preparation of nitrogen-containing bicyclic pyridine-based
derivs. as inhibitors of HMG CoA reductase)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:471999 CAPLUS Full-text
DN 143:13357
TI Combinations containing DPP IV inhibitors for treatment of obesity-related disorders
IN Holmes, David Grenville
PA Novartis A.-G., Switz.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005049088	A2	20050602	WO 2004-EP12989	20041116
	WO 2005049088	A3	20051229		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004290896	A1	20050602	AU 2004-290896	20041116
CA 2545514	A1	20050602	CA 2004-2545514	20041116
EP 1687030	A2	20060809	EP 2004-797931	20041116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
BR 2004016627	A	20070116	BR 2004-16627	20041116
CN 1901938	A	20070124	CN 2004-80040087	20041116
JP 2007511486	T	20070510	JP 2006-538824	20041116
MX 2006PA05596	A	20060811	MX 2006-PA5596	20060517
US 2007149451	A1	20070628	US 2007-579580	20070125
PRAI US 2003-520564P	P	20031117		
WO 2004-EP12989	W	20041116		

AB The present invention relates to a combination, such as a combined preparation or pharmaceutical composition, resp., comprising a dipeptidyl peptidase (DPP) IV inhibitor or a pharmaceutically acceptable salt thereof and an antiobesity agent, or an appetite regulating agent, or a pharmaceutically acceptable salt thereof. The present invention furthermore relates to the use of such a combination for the prevention, delay of progression or treatment of diseases and disorders selected from the group consisting of hypertension, congestive heart failure, left ventricular hypertrophy, peripheral arterial disease, diabetes, especially type 2 diabetes mellitus, diabetic retinopathy, macular degeneration, cataract, diabetic nephropathy, glomerulosclerosis, chronic renal failure, diabetic neuropathy, syndrome X, premenstrual syndrome, coronary heart disease, angina pectoris, thrombosis, atherosclerosis, myocardial infarction, transient ischemic attacks, stroke, vascular restenosis, hyperglycemia, hyperinsulinemia, hyperlipidemia, hypertryglyceridemia, insulin resistance, impaired glucose metabolism, conditions of impaired glucose tolerance, conditions of impaired fasting plasma glucose, obesity, erectile dysfunction, skin and connective tissue disorders, foot ulcerations and ulcerative colitis, endothelial dysfunction and impaired vascular compliance. For example, synergistic effects can be observed with the combination therapy of the DPP IV inhibitor LAF237 (10 μmole/kg) and an antiobesity agent (10 mg/kg) given orally for 3 wk on body weight, OGTT Glucose or insulin Excursions, and Plasma fibrinogen in rats.

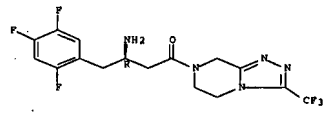
IT 654671-78-0, MK-0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing DPP IV inhibitors for treatment of obesity-related disorders)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 96 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:471952 CAPLUS Full-text
DN 143:20035
TI Combinations useful for the treatment of neuronal disorders
IN Schulz, Ingo; Schilling, Stephan; Niestroj, Andre Johannes; Demuth, Hans-Ulrich; Rossner, Steffen
PA Probiodrug A.G., Germany
SO PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005049027	A2	20050602	WO 2004-EP12301	20041029
WO 2005049027	A3	20060112		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004290499	A1	20050602	AU 2004-290499	20041029
CA 2544573	A1	20050602	CA 2004-2544573	20041029
EP 1680120	A2	20060719	EP 2004-791058	20041029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

JP 2007509898	T	20070419	JP 2006-537220	20041029
IN 2006KN01290	A	20070427	IN 2006-KN1290	20060516
PRAI US 2003-516717P	P	20031103		
WO 2004-EP12301	W	20041029		

OS MARPAT 143:20035
AB The present invention provides a method for the treatment of neuronal disorders, in a mammal such as a human, which method comprises administering an effective, non-toxic and pharmaceutically acceptable amount of at least one glutaminyl cyclase (QC)-inhibitor, optionally in combination with at least one agent, selected from the group consisting of prolyl endopeptidase inhibitor (PEP)-inhibitors, inhibitors of dipeptidyl peptidase IV (DP IV)/DP IV-like enzymes, NPY-receptor ligands, NPY agonists, NPY antagonists, acetylcholinesterase (ACE)-inhibitors, protein isoaspartate carboxymethyl transferase (PIMT) enhancers, inhibitors of β-secretases, inhibitors of γ-secretases and inhibitors of neutral endopeptidase, to a mammal in need thereof.

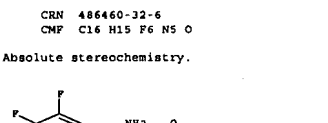
IT 654671-78-0, MK-0431
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibitor; treatment of neuronal disorders using glutaminyl cyclase inhibitors in combination with other agents)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 97 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:471947 CAPLUS Full-text
DN 143:1284
TI Use of organic compounds
IN Pratley, Richard; Foley, James E.; Hughes, Thomas Edward
PA Novartis A.-G., Swits.; Novartis Pharma G.m.b.H.
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005049022	A2	20050602	WO 2004-EP12990	20041116
WO 2005049022	A3	20050721		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004290897	A1	20050602	AU 2004-290897	20041116
CA 2545641	A1	20050602	CA 2004-2545641	20041116
EP 1686994	A2	20060809	EP 2004-797932	20041116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
BR 2004016628	A	20070116	BR 2004-16628	20041116
CN 1905876	A	20070131	CN 2004-80040508	20041116
JP 2007511487	T	20070510	JP 2006-538825	20041116
MX 2006PA05518	A	20060817	MX 2006-PA5518	20060516
IN 2006CN01724	A	20070629	IN 2006-CN1724	20060517
PRAI US 2003-520562P	P	20031117		
US 2003-520563P	P	20031117		
US 2004-547191P	P	20040224		
US 2004-547192P	P	20040224		
WO 2004-EP12990	W	20041116		

AB Disclosed is the use of a Dipeptidyl peptidase IV inhibitor (DPP-IV inhibitor), preferably (S)-1-[(3-hydroxy-1-adamantyl)amino]acetyl-2-cyano-pyrrolidine or a pharmaceutically acceptable salt thereof for the treatment of cardiovascular diseases or damages, renal diseases or damages, heart failure, or heart failure associated diseases.

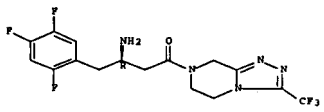
IT 654671-78-0, MK-0431
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DPP-IV inhibitors for treatment of cardiovascular and renal diseases)

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

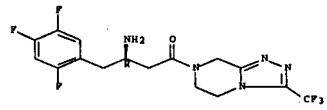
L11 ANSWER 98 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:419335 CAPLUS Full-text
DN 143:125519
TI MK-431 Merck
AU Deacon, Carolyn F.
CS Department of Medical Physiology Panum Institute, University of Copenhagen, Copenhagen N, DK-2200, Den.
SO Current Opinion in Investigational Drugs (Thomson Scientific) (2005), 6(4), 419-426
CODEN: COIDA2; ISSN: 1472-4472
PB Thomson Scientific
DT Journal; General Review
LA English
AB A review. Merck & Co is developing MK-431, the lead from a series of dipeptidyl peptidase IV inhibitors that enhance endogenous glucagon-like peptide-1 levels, for the potential treatment of type 2 diabetes. Phase III studies were initiated in the second quarter of 2004.
IT 654671-78-0, MK 431
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MK-431 for potential treatment of type 2 diabetic patients)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6

CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

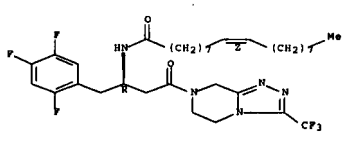
L11 ANSWER 99 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:405417 CAPLUS Full-text
DN 142:469248
TI Pharmaceutical compositions for enhanced absorption
IN Wong, Patrick S. L.; Yan, Dong
PA Alza Corporation, USA; Guittard, George V.
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005041925	A2	20050512	WO 2004-US36040	20041029
WO 2005041925	A3	20050929		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

AU 2004285533	A1	20050512	AU 2004-285533	20041029
CA 2543238	A1	20050512	CA 2004-2543238	20041029
US 2005158374	A1	20050721	US 2004-978141	20041029
US 2005163848	A1	20050728	US 2004-978136	20041029
US 2005163849	A1	20050728	US 2004-978137	20041029
US 2005163841	A1	20050728	US 2004-978138	20041029
US 2005165102	A1	20050728	US 2004-978139	20041029
US 2006094782	A9	20060504		
US 2005163850	A1	20050728	US 2004-978252	20041029
EP 1677757	A2	20060712	EP 2004-810118	20041029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1901881	A	20070124	CN 2004-80039649	20041029
JP 2007509973	T	20070419	JP 2006-538323	20041029
IN 2006KN01135	A	20070427	IN 2006-KN1135	20060502
NO 2006002504	A	20060721	NO 2006-2504	20060531
PRAI US 2003-516259P	P	20031031		
US 2003-519509P	P	20031112		
WO 2004-US36040	W	20041029		

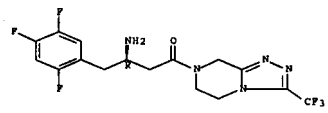
AB Disclosed is controlled delivery of pharmaceutical agents and methods, dosage forms and devices therefore. In particular, formulation, dosage forms, methods and devices for enhanced absorption and controlled delivery drug compds. are disclosed. Thus, metformin laurate was prepared and put into a dosage from containing PEG, PVP and Mg stearate.
IT 851476-07-8
RL: FMU (Formation, unclassified); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); PORM (Formation, nonpreparative); USES (Uses)
(pharmaceutical compns. for enhanced absorption)
RN 851476-07-8 CAPLUS
CN 9-Octadecenamide, N-[(1R)-3-(5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, (9Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 486460-32-6
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. for enhanced absorption)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 100 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:300188 CAPLUS Full-text
DN 142:360851
TI Novel crystalline form of a phosphate salt of a dipeptidyl peptidase-IV inhibitor
IN Chen, Alex M.; Wenslow, Robert M.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

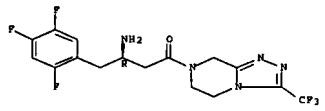
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005030127	A2	20050407	WO 2004-US30434	20040917
WO 2005030127	A3	20050526		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1667524	A2	20060614	EP 2004-784324	20040917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007021430	A1	20070125	US 2006-570409	20060303
PRAI US 2003-505118P	P	20030923		
WO 2004-US30434	W	20040917		

AB The present invention relates to a novel crystalline anhydrate polymorph of the dihydrogen phosphate salt of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine as well as a process for their preparation, pharmaceutical compns. containing this form, and methods of use of the form for the treatment of diabetes, obesity, and high blood pressure.
IT 654671-77-9P 654671-78-0P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline form of phosphate salt of dipeptidyl peptidase-IV inhibitor)
RN 654671-77-9 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

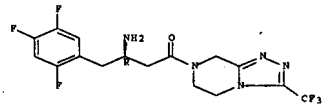
CRN 7664-38-2
CMF H3 O4 P

RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.

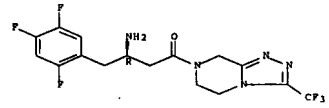


CM 2

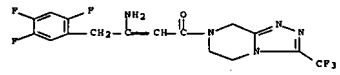
CRN 7664-38-2
CMF H3 O4 P

IT 486460-32-6P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(crystalline form of phosphate salt of dipeptidyl peptidase-IV inhibitor)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 847445-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystalline form of phosphate salt of dipeptidyl peptidase-IV inhibitor)
RN 847445-81-2 CAPLUS
CN 2-Buten-1-one, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)- (CA INDEX NAME)



L11 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:216618 CAPLUS Full-text
DN 142:303604
TI Novel crystal forms of a dihydrogen phosphate salt of a trizolopyrazine

dipeptidyl peptidase IV inhibitor
IN Wenslow, Robert M.; Armstrong, Joseph D., III; Chen, Alex M.; Cypes, Stephen; Ferlita, Russell R.; Hansen, Karl; Lindemann, Christopher M.; Spartalis, Evangelia
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005020920	A2	20050310	WO 2004-US27983	20040827
WO 2005020920	A3	20050428		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004268024	A1	20050310	AU 2004-268024	20040827
AU 2004268024	B2	20070712		
CA 2536251	A1	20050310	CA 2004-2536251	20040827
EP 1662876	A2	20060607	EP 2004-782460	20040827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1845674	A	20061011	CN 2004-80025043	20040827
JP 2007504230	T	20070301	JP 2006-525371	20040827
US 2006287528	A1	20061221	US 2006-569566	20060227
PRAI US 2003-499629P	P	20030902		
WO 2004-US27983	W	20040827		

OS CASREACT 142:303604
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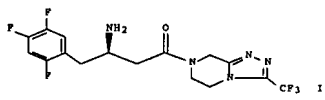
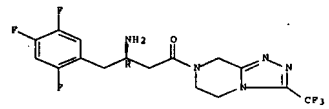


AB The present invention relates to crystalline anhydrate polymorphs of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3- α]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine dihydrogen phosphate salt (I) as well as a process for their preparation, pharmaceutical compns. containing these novel forms, and methods of use of the novel forms and pharmaceutical compns. for the treatment of diabetes, obesity, and high blood pressure.

IT 486460-32-6P 654671-78-0P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal forms of a trizolopyrazine dihydrogen phosphate salt dipeptidyl peptidase IV inhibitor)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

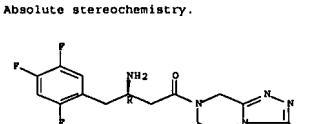


RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.

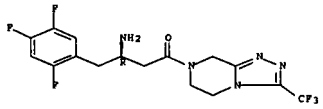


CM 2

CRN 7664-38-2
CMF H3 O4 P

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.

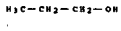


CM 2

CRN 7664-38-2
CMF H3 O4 P

CM 3

CRN 71-23-8
CMF C3 H8 O

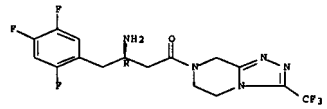


RN 847445-80-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate, compd. with 2-propanol (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.

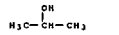


CM 2

CRN 7664-38-2
CMF H3 O4 P

CM 3

CRN 67-63-0
CMF C3 H8 O



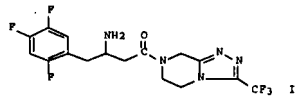
L11 ANSWER 102 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2005:29336 CAPLUS Full-text
DN 142:114455
TI Preparation of phosphoric acid salt of a β-amino acid amide dipeptidyl peptidase-IV inhibitor and its monohydrate
IN Cypes, Stephen Howard; Chen, Alex Minhua; Ferlita, Russell R.; Hansen, Karl; Lee, Ivan; Vydra, Vicky K.; Wenslow, Robert M., Jr.
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005003135	A1	20050113	WO 2004-US19683	20040618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,				

LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004253889	A1	20050113	AU 2004-253889	20040618
CA 2529400	A1	20050113	CA 2004-2529400	20040618
EP 1654263	A1	20060510	EP 2004-755691	20040618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2006516268	T	20060629	JP 2005-518292	20040618
BR 2004011726	A	20060808	BR 2004-11726	20040618
CN 1832949	A	20060913	CN 2004-80017544	20040618
US 2005032804	A1	20050210	US 2004-874992	20040623
MX 2005PA13931	A	20060224	MX 2005-PA13931	20051219
NO 2006000362	A	20060323	NO 2006-362	20060123
PRAI US 2003-482161P	P	20030624		
WO 2004-US19683	W	20040618		

GI



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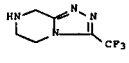
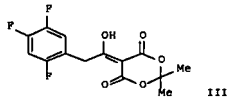


II



III

AB The invention is related to the preparation of dihydrogenphosphate salt of 4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin- 7(8H)-yl]-1-(2,4,5- trifluorophenyl)butan-2-amine (I•H3PO4) which is a potent inhibitor of dipeptidyl peptidase-IV and therefore useful for the prevention and/or treatment of type 2 diabetes. The invention also relates to the preparation of hydrates, in particular a crystalline monohydrate of the dihydrogenphosphate salt I, its pharmaceutical compns., and methods of use for the treatment of diabetes, obesity, and high blood pressure. Thus, treating II•HCl (preparation given) with III (preparation given), followed by reaction with NH4OAc in MeOH, and hydrogenation gave amine (R)-I. Reaction of amine

(R)-I with 85% aqueous H3PO4 and recrystn. from isopropanol/water gave (R)-I•H3PO4•H2O.

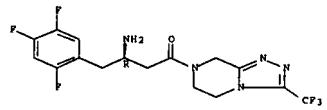
IT 654671-77-9P, (2R)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine dihydrogen phosphate monohydrate
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(DPPIV inhibitor; preparation of triazolopyrazine beta amino amide dihydrogenphosphates and their monohydrates as peptidase-iv inhibitor)

RN 654671-77-9 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate, hydrate (1:1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



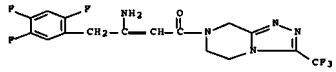
CM 2

CRN 7664-38-2
CMF H3 O4 P

IT 486460-32-6P, (2R)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine 767340-03-4P, (2Z)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)but-2-en-2-amine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of triazolopyrazine beta amino amide dihydrogenphosphates and their monohydrates as peptidase-iv inhibitor)

RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-

IT 847445-81-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(crystal forms of a trizolopyrazine dihydrogen phosphate salt dipeptidyl peptidase IV inhibitor)
RN 847445-81-2 CAPLUS
CN 2-Buten-1-one, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)- (CA INDEX NAME)

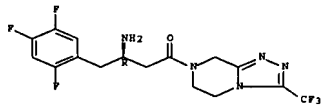


IT 847445-75-4 847445-76-5 847445-77-6
847445-78-7 847445-79-8 847445-80-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystal forms of a trizolopyrazine dihydrogen phosphate salt dipeptidyl peptidase IV inhibitor)
RN 847445-75-4 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate, compd. with 2-propanone (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

CM 3

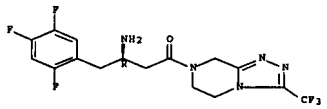
CRN 67-64-1
CMF C3 H6 O

RN 847445-76-5 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate, compd. with acetonitrile (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

CM 3

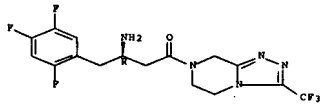
CRN 75-05-8
CMF C2 H3 N

RN 847445-77-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate, compd. with methanol (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

CM 3

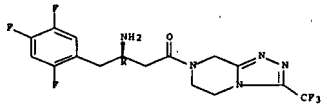
CRN 67-56-1
CMF C H4 O

RN 847445-78-7 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate, compd. with ethanol (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

CM 3

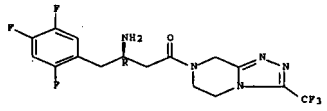
CRN 64-17-5
CMF C2 H6 O

RN 847445-79-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate, compd. with 1-propanol (1:1:?) (9CI) (CA INDEX NAME)

CM 1

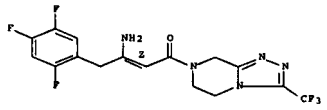
a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 767340-03-4 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(2Z)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)-2-butenyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

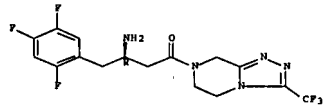


IT 654671-78-0P 823817-57-8P 823817-58-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of triazolopyrazine beta amino amide dihydrogenphosphates and their monohydrates as peptidase-iv inhibitor)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



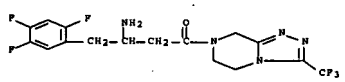
CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 823817-57-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 823817-56-7
CMF C16 H15 F6 N5 O



CM 2

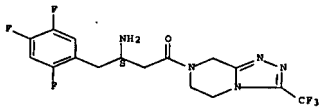
CRN 7664-38-2
CMF H3 O4 P

RN 823817-58-9 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3S)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, phosphate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 823817-55-6
CMF C16 H15 F6 N5 O

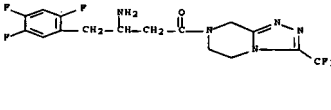
Absolute stereochemistry.



CM 2

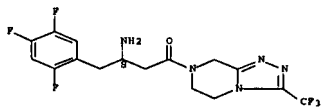
CRN 7664-38-2
CMF H3 O4 P

IT 823817-56-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of triazolopyrazine beta amino amide dihydrogenphosphates and their monohydrates as peptidase-iv inhibitor)
RN 823817-56-7 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)



IT 823817-55-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of triazolopyrazine beta amino amide dihydrogenphosphates and their monohydrates as peptidase-iv inhibitor)
RN 823817-55-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3S)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 103 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1124587 CAPLUS Full-text
DN 142:69188
TI Combination therapy for the treatment of diabetes
IN Erondu, Ngozi E.; Fong, Tung M.; MacNeil, Douglas J.; Van Der Ploeg, Leonardus H. T.; Kanatani, Akio
PA Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.
SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004110375	A2	20041223	WO 2004-US17291	20040602
	WO 2004110375	A3	20050512		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1635832	A2	20060322	EP 2004-753999	20040602
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	US 2007099884	A1	20070503	US 2005-559206	20051202
PRAI	US 2003-476388P	P	20030606		
	WO 2004-US17291	W	20040602		

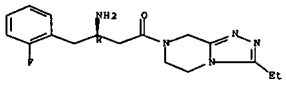
OS MARPAT 142:69188

AB The present invention relates to compns. comprising an anti-obesity agent and an anti-diabetic agent useful for the treatment of diabetes, diabetes associated with obesity and diabetes-related disorders. The present invention further relates to methods of treating or preventing obesity, and obesity-related disorders, in a subject in need thereof by administering a composition of the present invention. The present invention further provides for pharmaceutical compns., medicaments, and kits useful in carrying out these methods.

IT 486459-82-9 486459-83-0 486459-84-1
486459-85-2 486459-88-5 486459-89-6
486459-97-6 486460-31-5 486460-32-6
487064-52-8 487064-54-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibitor; combination therapy of diabetes and diabetes-related disorders using antiobesity agent and antidiabetic agent and other agents)

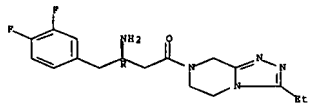
RN 486459-82-9 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2-fluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



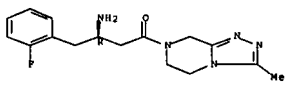
RN 486459-83-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



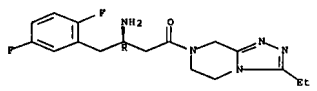
RN 486459-84-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2-fluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



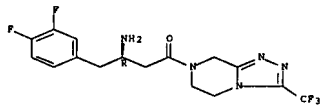
RN 486459-85-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



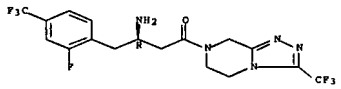
RN 486459-88-5 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



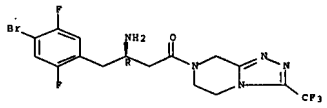
RN 486459-89-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-[2-fluoro-4-(trifluoromethyl)phenyl]-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



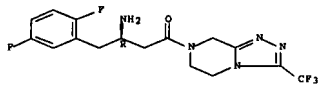
RN 486459-97-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(4-bromo-2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



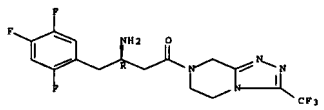
RN 486460-31-5 CAPLUS
CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



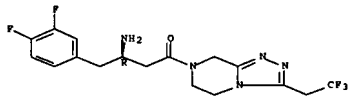
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



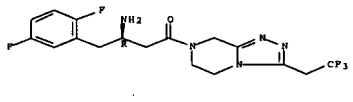
RN 487064-52-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

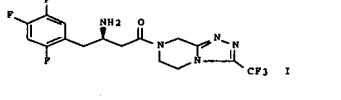


RN 487064-54-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 104 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:1070488 CAPLUS Full-text
DN 142:198023
TI (2R)-4-Oxo-4-[3-(Trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine: A Potent, Orally Active Dipeptidyl Peptidase IV Inhibitor for the Treatment of Type 2 Diabetes
AU Kim, Dooseop; Wang, Liping; Beconi, Maria; Eiermann, George J.; Fisher, Michael H.; He, Huaibing; Hickey, Gerard J.; Kowalchick, Jennifer E.; Leiting, Barbara; Lyons, Kathryn; Marsilio, Frank; McCann, Margaret E.; Patel, Reshma A.; Petrov, Aleksandr; Scapin, Giovanna; Patel, Sangita B.; Roy, Ranabir Sinha; Wu, Joseph K.; Wyvratt, Matthew J.; Zhang, Bei B.; Zhu, Lan; Thornberry, Nancy A.; Weber, Ann E.
CS Merck Research Laboratories, Merck & Co., Inc., Rahway, NJ, 07065, USA
SO Journal of Medicinal Chemistry (2005), 48(1), 141-151
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 142:198023
GI



I

AB A novel series of β-amino amides incorporating fused heterocycles, i.e., triazolopiperazines, were synthesized and evaluated as inhibitors of dipeptidyl peptidase IV (DPP-IV) for the treatment of type 2 diabetes. (2R)-4-Oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]triazolo[4,3-a]pyrazin- 7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine (I) is a potent, orally active DPP-IV inhibitor (IC50 = 18 nM) with excellent selectivity over other proline-selective peptidases, oral bioavailability in preclin. species, and in vivo efficacy in animal models. MK-0431, the phosphate salt of I, was selected for development as a potential new treatment for type 2 diabetes.

IT 654671-78-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(MK-0431; preparation of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))

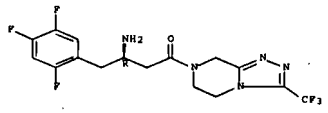
RN 654671-78-0 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

IT 837430-29-2P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro(fluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine bound to dipeptidyl peptidase IV)

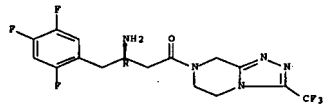
RN 837430-29-2 CAPLUS

CN Peptidase, dipeptidyl, IV, compd. with 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

CRN 54249-88-6
CMF Unspecified
CCI MAN

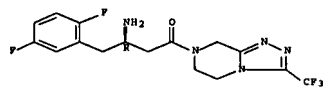
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 486460-31-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [(R)-(amino)(difluorophenyl)(oxo)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine and its salts)

RN 486460-31-5 CAPLUS

CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 837430-23-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of [(R)-(amino)(difluorophenyl)(oxo)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine and its salts)

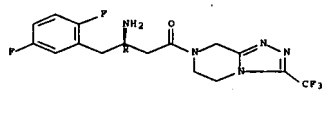
RN 837430-23-6 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-31-5
CMF C16 H16 F5 N5 O

Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

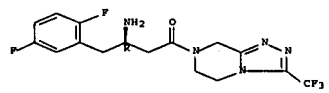
Double bond geometry as shown.

IT 486459-70-5P 837430-22-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(R)-(amino)(difluorophenyl)(oxo)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))

RN 486459-70-5 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

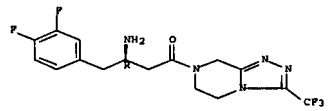


● HCl

RN 837430-22-5 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



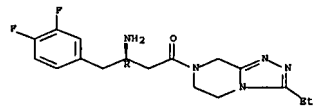
● HCl

IT 486459-69-2P 837430-21-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(R)-(amino)(difluorophenyl)(oxo)butyl]tetrahydro-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))

RN 486459-69-2 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro-, dihydrochloride (9CI) (CA INDEX NAME)

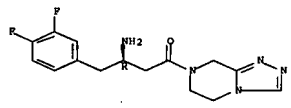
Absolute stereochemistry.



●2 HCl

RN 837430-21-4 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-, dihydrochloride (9CI) (CA INDEX NAME)

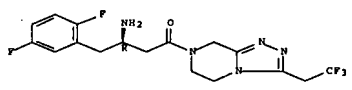
Absolute stereochemistry.



●2 HCl

IT 837430-27-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(R)-(amino)(oxo)(difluorophenyl)butyl]tetrahydro(fluoroethyl)-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))
RN 837430-27-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(2,2,2-trifluoroethyl)-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

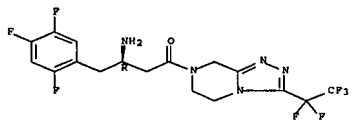


●2 HCl

IT 837430-26-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro(fluoroethyl)-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))
RN 837430-26-9 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(pentafluoroethyl)-,

monohydrochloride (9CI) (CA INDEX NAME)

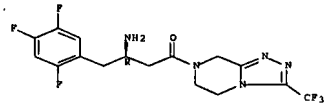
Absolute stereochemistry.



● HCl

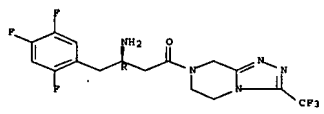
IT 486460-32-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



IT 486459-71-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))
RN 486459-71-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



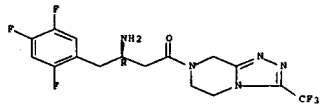
● HCl

IT 837430-24-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine salt)
RN 837430-24-7 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

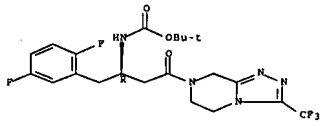
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

IT 486460-22-4P 486460-23-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

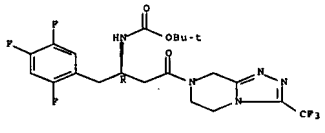
(preparation of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine using protected derivative as synthetic intermediate)
RN 486460-22-4 CAPLUS
CN Carbamic acid, [(1R)-1-[(2,5-difluorophenyl)methyl]-3-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



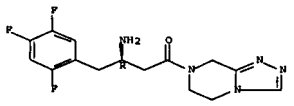
RN 486460-23-5 CAPLUS
CN Carbamic acid, [(1R)-3-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 837430-25-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of [(R)-(amino)(oxo)(trifluorophenyl)butyl]tetrahydro-1,2,4-triazolo[4,3-a]pyrazine and study of its activity as orally active dipeptidyl peptidase IV inhibitor (antidiabetic))
RN 837430-25-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-, dihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●2 HCl

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:964805 CAPLUS Full-text
DN 141:388745
TI Preparation of glutaminyl cyclase inhibitors for use in treating neurological diseases
IN Schilling, Stephan; Niestroj, Andre J.; Heiser, Ulrich; Buchholz, Mirko; Demuth, Hans-Ulrich
PA Probiodrug AG, Germany
SO U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004224875	A1	20041111	US 2004-838993	20040505
WO 2004098591	A2	20041118	WO 2004-EP4773	20040505
WO 2004098591	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1620091	A2	20060201	EP 2004-731158	20040505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
JP 2006525276	T	20061109	JP 2006-505375	20040505
AU 2005210004	A1	20050818	AU 2005-210004	20050204
CA 2554809	A1	20050818	CA 2005-2554809	20050204
WO 2005075436	A2	20050818	WO 2005-EP1153	20050204
WO 2005075436	A3	20051208		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

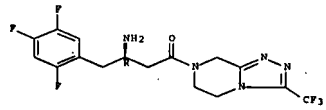
US 2005215573	A1	20050929	US 2005-51760	20050204
EP 1713780	A2	20061025	EP 2005-707206	20050204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
CN 1918131	A	20070221	CN 2005-80004289	20050204
BR 2005007485	A	20070710	BR 2005-7485	20050204
JP 2007520520	T	20070726	JP 2006-551809	20050204
MX 2006PA08868	A	20061030	MX 2006-PA8868	20060804
PRAI US 2003-468014P	P	20030505		
US 2004-542133P	P	20040205		
US 2004-838993	A	20040505		
WO 2004-EP4773	W	20040505		
US 2004-634364P	P	20041208		
WO 2005-EP1153	W	20050204		

OS MARPAT 141:388745
AB The present invention relates to compds. that act as inhibitors of QC and combinations thereof for the treatment of neuronal disorders, especially Alzheimer's disease, Down's syndrome, Parkinson's disease, Huntington's chorea, pathogenic psychotic conditions, schizophrenia, impaired food intake, sleep-wakefulness, impaired homeostatic regulation of energy metabolism, impaired autonomic function, impaired hormonal balance, impaired regulation, body fluids, hypertension, fever, sleep dysregulation, anorexia, anxiety related disorders including depression, seizures including epilepsy, drug withdrawal and alcoholism, neurodegenerative disorders including cognitive dysfunction and dementia.
IT 654671-78-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(in combination chemotherapy; preparation of glutaminyl cyclase inhibitors for use in treating neurol. diseases)
RN 654671-78-0 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)-, phosphate (1:1) (CA INDEX NAME)

CM 1

CRN 486460-32-6
CMF C16 H15 F6 N5 O

Absolute stereochemistry.



CM 2

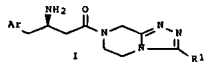
CRN 7664-38-2
CMF H3 O4 P

L11 ANSWER 106 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:857554 CAPLUS Full-text
DN 141:314625
TI Process for the preparation of β-amino acid amide dipeptidyl peptidase-IV inhibitors
IN Angelaud, Remy; Armstrong, Joseph D., III; Askin, David; Balsells, Jaume; Hansen, Karl; Lee, Jaemoon; Maligres, Peter E.; Rivera, Nelo R.; Xiao, Yi; Zhong, Yong-Li
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004087650	A2	20041014	WO 2004-US8826	20040323
WO 2004087650	A3	20050113		

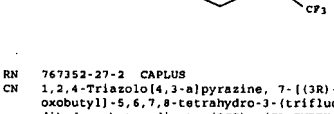
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2003-457976P P 20030327
OS CASREACT 141:314625; MARPAT 141:314625
GI



AB The invention provides a novel process for the preparation of chiral β-amino acid amides I (Ar is Ph which may be substituted by halogen, trifluoromethyl or trifluoromethoxy; R1 is H, alkyl or fluoroalkyl) which are inhibitors of dipeptidyl peptidase-IV and thereby useful for the treatment of Type 2 diabetes. The process involves acylation of 5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine (II) or a derivative with a (3R)-3-[(benzyloxy)amino]-4-arylbutanoic acid (III), followed by hydrogenolysis. In an example, I (Ar = 2,5-difluorophenyl, R1 = CF3) was prepared from II.HCl 3-trifluoromethyl derivative (prepared from hydrazine, Et trifluoroacetate, chloroacetyl chloride, and ethylenediamine) and III (Ar = 2,5-difluorophenyl) prepared from 2,5-difluorophenylacetic acid, Meldrum's acid, and O-benzylhydroxylamine hydrochloride.
IT 486460-32-6P 767352-27-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for preparation of triazolopyrazine β-amino acyl derivs. as dipeptidyl peptidase-IV inhibitors)
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

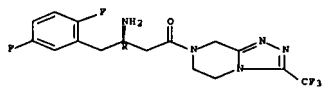


RN 767352-27-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (2R,3R)-2,3-dihydroxybutanedioate (9CI) (CA INDEX NAME)

CM 1

CRN 486460-31-5
CMF C16 H16 F5 N5 O

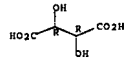
Absolute stereochemistry.



CM 2

CRN 87-69-4
CMF C4 H6 O6

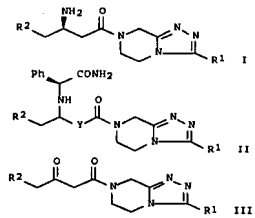
Absolute stereochemistry.



L11 ANSWER 107 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:824045 CAPLUS Full-text
DN 141:332476
TI Process for preparation of chiral β-amino acid derivatives
IN Dreher, Spencer D.; Ikemoto, Norihiro; Njolito, Eugenia; Rivera, Nelo R.; Tellers, David M.; Xiao, Yi
PA Merck & Co., Inc, USA
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

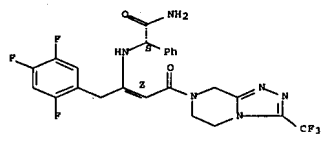
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004085661	A2	20041007	WO 2004-US8533	20040319
WO 2004085661	A3	20050310		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI US 2003-457128P	P	20030324		
US 2003-511210P	P	20031015		

OS CASREACT 141:332476; MARPAT 141:332476
GI



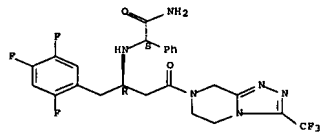
AB A process for the asym. synthesis of enantiomerically enriched β-amino acid derivs. I [R1 = H, or alkyl, unsubstituted or substituted with one to five fluorines; R2 = Ph, unsubstituted or independently substituted with one to five substituents; fluorine, trifluoromethyl, or trifluoromethoxy] in a suitable organic solvent is developed, with includes catalytic hydrogenation of Z-enamines II (Y = :CH), which was prepared by addition of L-phenylglycine amide to β-ketoesters III under acidic conditions, and subsequent catalytic hydrogenolysis of II (Y = CH2). Thus, β-ketoester III (R1 = CF3; R2 = 2,4,5-trifluorophenyl) obtained from 2,4,5-trifluorophenylacetic acid and 3-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[4,4- α]pyrazine hydrochloride was added to L-phenylglycine amide to give Z-enamine II (R1 = CF3; R2 = 2,4,5-trifluorophenyl), which after catalytic hydrogenation in the presence of platinum dioxide, followed by hydrogenolysis with palladium dihydroxide as catalyst gave compound I (R1 = CF3; R2 = 2,4,5-trifluorophenyl) in 94.55% yield and 97% ee.
IT 769195-19-9P 769195-20-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of chiral β-amino acid derivs. via addition of phenylglycine amide to triazolopyrazinyl β-ketoesters, followed by catalytic hydrogenation of enamines and catalytic hydrogenolysis)
RN 769195-19-9 CAPLUS
CN Benzeneacetamide, α-[[(1Z)-3-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]-1-propenyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



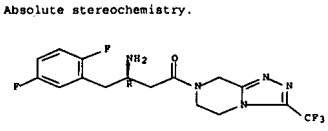
RN 769195-20-2 CAPLUS
CN Benzeneacetamide, α-[[(1R)-3-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



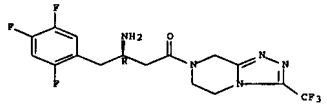
IT 486460-31-5P 486460-32-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. synthesis of chiral β-amino acid derivs. via addition of phenylglycine amide to triazolopyrazinyl β-ketoesters, followed by catalytic hydrogenation of enamines and catalytic hydrogenolysis)
RN 486460-31-5 CAPLUS
CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 108 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2004:817850 CAPLUS Full-text
DN 141:314350
TI Process for the preparation of chiral β-amino acid derivatives by asymmetric hydrogenation of enamino esters and amides using transition-metal complexed chiral ferrocenyldiphosphines.
IN Xiao, Yi; Armstrong, Joseph D., III; Krska, Shane W.; Njolito, Eugenia; Rivera, Nelo R.; Sun, Yongkui; Rosner, Thorsten
PA Merck & Co. Inc., USA
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004085378	A1	20041007	WO 2004-US7793	20040315
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004223885	A1	20041007	AU 2004-223885	20040315
CA 2518435	A1	20041007	CA 2004-2518435	20040315
EP 1606243	A1	20051221	EP 2004-720790	20040315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
CN 1761642	A	20060419	CN 2004-80007313	20040315
JP 2006521354	T	20060921	JP 2006-507177	20040315
US 2006194977	A1	20060831	US 2005-549425	20050915
PRAI US 2003-455932P	P	20030319		
WO 2004-US7793	A	20040315		

OS CASREACT 141:314350; MARPAT 141:314350
AB (R)- or (S)-R1CH(NH2)CH2CO2Z [Z = OR2, SR2, NR2R3; R1 = alkyl, aryl, heteroaryl, aralkyl, heteroaralkyl; R2, R3 = H, alkyl, aryl, aralkyl; R2R3N = (substituted) 4-7 membered ring] were prepd in ≥70% enantiomeric excess by hydrogenation of prochiral R1(H2N)C:CCO2Z (variables as above) in the presence of transition-metal complexed chiral ferrocenyldiphosphines in a suitable

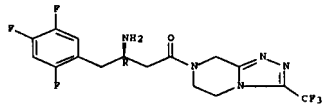
organic solvent. Thus, (Z)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro-1,2,4-triazolo[4,3-a]pyrazin- 7(8H)-yl]-1-(2,4,5-trifluorophenyl)but-2-en-2-amine (preparation given) was hydrogenated in the presence of chloro(1,5-cyclooctadiene)rhodium(I) dimer and (R,S) tert-Bu Josiphos in MeOH at 200 psi and 50° for 13 h to give 72% (R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro-1,2,4-triazolo[4,3- a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine in 98-99% enantiomeric excess.

IT 486460-32-6P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of chiral β-amino acid derivs. by asym. hydrogenation of enamino esters and amides using transition-metal complexed chiral ferrocenyldiphosphines)

RN 486460-32-6 CAPLUS

CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.

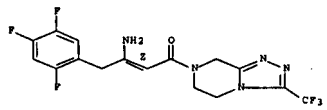


IT 767340-03-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of chiral β-amino acid derivs. by asym. hydrogenation of enamino esters and amides using transition-metal complexed chiral ferrocenyldiphosphines)

RN 767340-03-4 CAPLUS

CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(2Z)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)-2-butenyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 109 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN

AN 2004:331907 CAPLUS Full-text

DN 140:357376

TI Preparation of aminoacyl triazolopyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes

IN Kim, Dooseop; Kowalchick, Jennifer E.

PA Merck & Co., Inc., USA

SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2

DT Patent

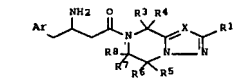
LA English

FAN.CNT 1

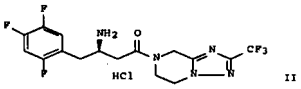
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004032836	A2	20040422	WO 2003-US31287	20031003
WO 2004032836	A3	20040610		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2499586	A1	20040422	CA 2003-2499586	20031003
AU 2003275404	A1	20040504	AU 2003-275404	20031003
EP 1554280	A2	20050720	EP 2003-759681	20031003
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006504732	T	20060209	JP 2004-543095	20031003
US 2006014953	A1	20060119	US 2005-530215	20050404
PRAI US 2002-416558P	P	20021007		
WO 2003-US31287	W	20031003		

OS MARPAT 140:357376

GI



I



II

AB The title compds. I [X = N or CR2; R1, R2 = H, halo, cyano, (substituted)alkyl, (substituted)alkoxy, (substituted)alkylthio, (substituted)alkenyl, etc.; R3, R4, R5, R6, R7, R8 = H, cyano, (CH2)nCOOH,

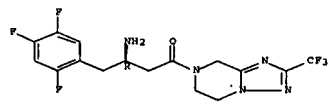
(CH2)nCOO-alkyl, alkyl, (CH2)n-(hetero)aryl, (CH2)n-heterocyclyl, etc.; n = 0-2] were prepared as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes. Thus, reaction of 2-(trifluoromethyl)-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-a]pyrazine (preparation given) with (3R)-3-[(tert-butoxycarbonyl)amino]-4-(2,4,5-trifluorophenyl)butanoic acid (preparation given) followed by the treatment of hydrochloric acid yielded compound II. The prepared compds. were effective in inhibiting the dipeptidyl peptidase-IV enzyme with an IC50 of less than 1 μM.

IT 681249-20-7P 681249-22-9P 681249-24-1P
681249-26-3P 681249-28-5P 681249-30-9P
681249-31-0P 681249-33-2P 681249-34-3P
681249-35-4P 681249-36-5P 681249-37-6P
681249-38-7P 681249-39-8P 681249-40-1P
681249-41-2P 681249-42-3P 681249-43-4P
681249-44-5P 681249-45-6P 681249-46-7P
681249-47-8P 681249-48-9P 681249-49-0P
681249-50-3P 681249-51-4P 681249-53-6P
681249-54-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Preparation of aminoacyl triazolopyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes)

RN 681249-20-7 CAPLUS

CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

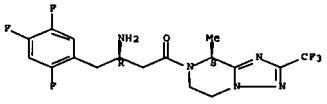


● HCl

RN 681249-22-9 CAPLUS

CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-methyl-2-(trifluoromethyl)-, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

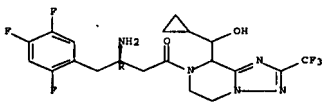


● HCl

RN 681249-24-1 CAPLUS

CN [1,2,4]Triazolo[1,5-a]pyrazine-8-methanol, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-α-cyclopropyl-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

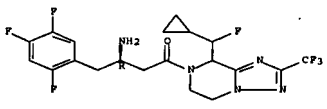


● HCl

RN 681249-26-3 CAPLUS

CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-8-(cyclopropylfluoromethyl)-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



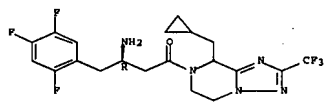
● HCl

RN 681249-28-5 CAPLUS

CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-

trifluorophenyl)butyl]-8-(cyclopropylmethyl)-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

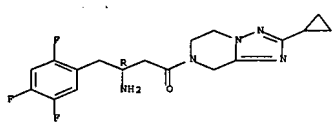
Absolute stereochemistry.



● HCl

RN 681249-30-9 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-2-cyclopropyl-5,6,7,8-tetrahydro-, monohydrochloride (9CI) (CA INDEX NAME)

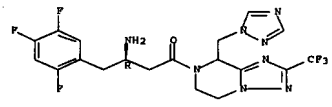
Absolute stereochemistry.



● HCl

RN 681249-31-0 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-(1H-1,2,4-triazol-1-ylmethyl)-2-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



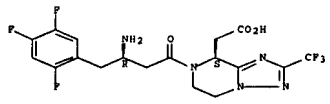
● HCl

RN 681249-33-2 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetic acid, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, (8S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 681249-32-1
CMF C18 H17 F6 N5 O3

Absolute stereochemistry.

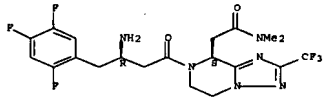


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 681249-34-3 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetamide, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-N,N-dimethyl-2-(trifluoromethyl)-, monohydrochloride, (8S)- (9CI) (CA INDEX NAME)

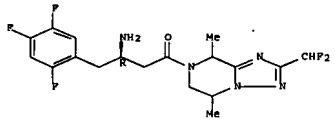
Absolute stereochemistry.



● HCl

RN 681249-35-4 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-2-(difluoromethyl)-5,6,7,8-tetrahydro-5,8-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

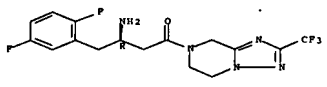
Absolute stereochemistry.



● HCl

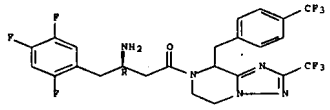
RN 681249-36-5 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



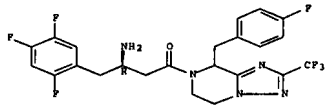
RN 681249-37-6 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-8-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



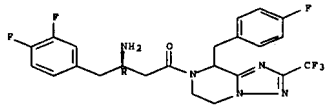
RN 681249-38-7 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-8-[(4-fluorophenyl)methyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



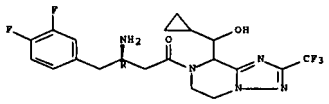
RN 681249-39-8 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-8-[(4-fluorophenyl)methyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



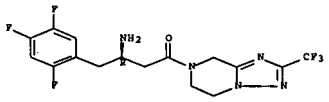
RN 681249-40-1 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-methanol, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-α-cyclopropyl-5,6,7,8-tetrahydro-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



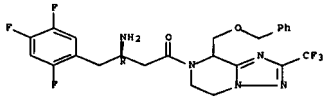
RN 681249-41-2 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



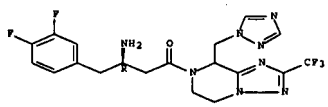
RN 681249-42-3 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-[(phenylmethoxy)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



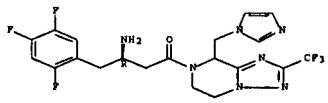
RN 681249-43-4 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-8-(1H-1,2,4-triazol-1-ylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



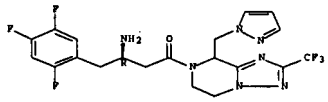
RN 681249-44-5 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-(1H-imidazol-1-ylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



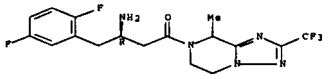
RN 681249-45-6 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-(1H-pyrazol-1-ylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



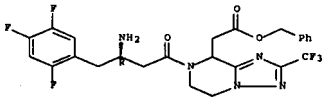
RN 681249-46-7 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-8-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



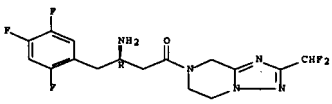
RN 681249-47-8 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetic acid, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



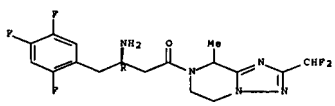
RN 681249-48-9 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-2-(difluoromethyl)-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



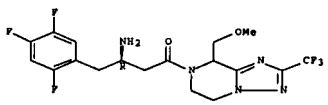
RN 681249-49-0 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-2-(difluoromethyl)-5,6,7,8-tetrahydro-8-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



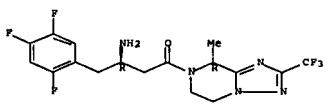
RN 681249-50-3 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-(methoxymethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 681249-51-4 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-methyl-2-(trifluoromethyl)-, monohydrochloride, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

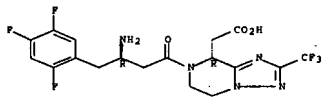
RN 681249-53-6 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetic acid, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, (8R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 681249-52-5

CMF C18 H17 F6 N5 O3

Absolute stereochemistry.

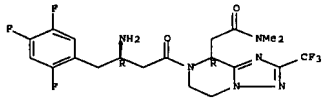


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 681249-54-7 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetamide, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-N,N-dimethyl-2-(trifluoromethyl)-, monohydrochloride, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



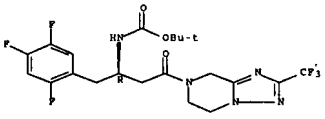
● HCl

IT 681249-58-1P 681249-62-7P 681249-63-8P
681249-66-1P 681249-69-4P 681249-73-0P
681249-80-9P 681249-87-6P 681249-89-8P
681249-91-2P 681249-94-5P 681249-99-0P
681250-01-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(Preparation of aminoacyl triazolopyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes)

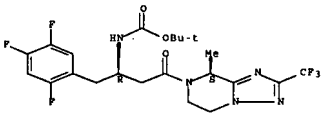
RN 681249-58-1 CAPLUS
CN Carbamic acid, [(1R)-3-[5,6-dihydro-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



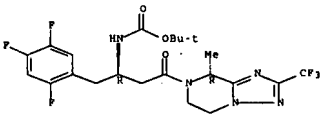
RN 681249-62-7 CAPLUS
CN Carbamic acid, [(1R)-3-[(8S)-5,6-dihydro-8-methyl-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



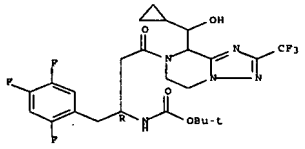
RN 681249-63-8 CAPLUS
CN Carbamic acid, [(1R)-3-[(8R)-5,6-dihydro-8-methyl-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



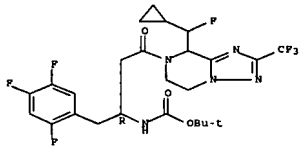
RN 681249-66-1 CAPLUS
CN Carbamic acid, [(1R)-3-[8-(cyclopropylhydroxymethyl)-5,6-dihydro-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



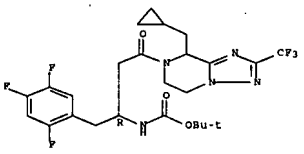
RN 681249-69-4 CAPLUS
CN Carbamic acid, [(1R)-3-[8-(cyclopropylfluoromethyl)-5,6-dihydro-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



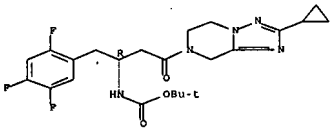
RN 681249-73-0 CAPLUS
CN Carbamic acid, [(1R)-3-[8-(cyclopropylmethyl)-5,6-dihydro-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



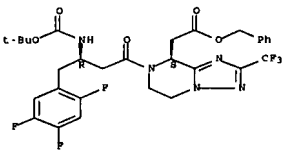
RN 681249-80-9 CAPLUS
CN Carbamic acid, [(1R)-3-(2-cyclopropyl-5,6-dihydro[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 681249-87-6 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetic acid, 7-[(3R)-3-[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, phenylmethyl ester, (8S)- (9CI) (CA INDEX NAME)

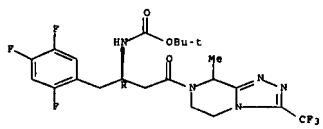
Absolute stereochemistry.



RN 681249-89-8 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetic acid, 7-[(3R)-3-amino-1-oxo-4-

NAME)

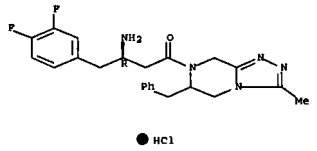
Absolute stereochemistry.



IT 611239-94-2P 611239-96-4P 611240-01-8P
611240-02-9P 611240-03-0P 611240-04-1P
611240-21-2P 611240-22-3P 611240-23-4P
611240-24-5P 611240-26-7P 611240-27-8P
611240-39-2P 611240-40-5P 611240-41-6P
611240-42-7P 611240-43-8P 611240-44-9P
611240-45-0P 611240-80-3P 611240-88-1P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoacylimidazo- and triazolopyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes)

RN 611239-94-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-methyl-6-(phenylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



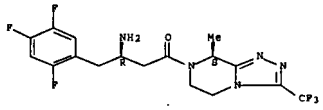
● HCl

RN 611239-96-4 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-methyl-3-(trifluoromethyl)-, (8S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 611239-95-3
CMF C17 H17 F6 N5 O

Absolute stereochemistry.

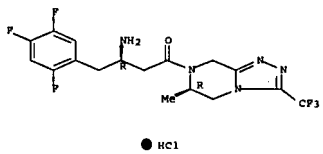


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 611240-01-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-6-methyl-3-(trifluoromethyl)-, monohydrochloride, (6R)- (9CI) (CA INDEX NAME)

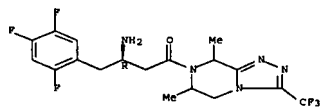
Absolute stereochemistry.



● HCl

RN 611240-02-9 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-6,8-dimethyl-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

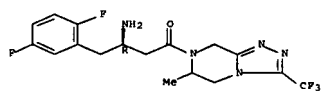
Absolute stereochemistry.



● HCl

RN 611240-03-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-6-methyl-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

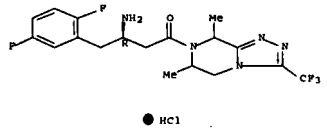
Absolute stereochemistry.



● HCl

RN 611240-04-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-6,8-dimethyl-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

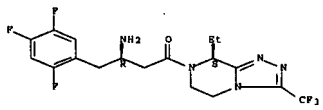
Absolute stereochemistry.



● HCl

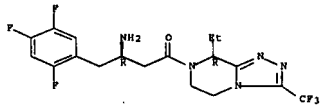
RN 611240-21-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-8-ethyl-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



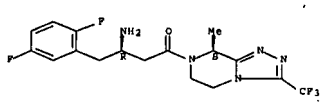
RN 611240-22-3 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-8-ethyl-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (8R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 611240-23-4 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-8-methyl-3-(trifluoromethyl)-, (8S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 611240-24-5 CAPLUS
CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[(8R)-5,6-dihydro-8-methyl-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

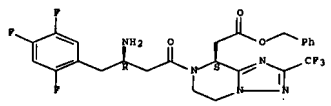
Absolute stereochemistry.

(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, phenylmethyl ester, (8S)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 681249-88-7
CMF C25 H23 F6 N5 O3

Absolute stereochemistry.



CM 2

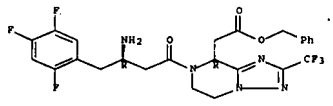
CRN 76-05-1
CMF C2 H F3 O2

RN 681249-91-2 CAPLUS
CN [1,2,4]Triazolo[1,5-a]pyrazine-8-acetic acid, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-2-(trifluoromethyl)-, phenylmethyl ester, (8R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 681249-90-1
CMF C25 H23 F6 N5 O3

Absolute stereochemistry.

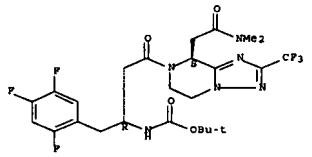


CM 2

CRN 76-05-1
CMF C2 H F3 O2

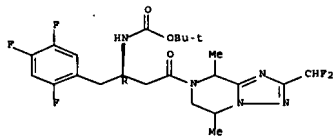
RN 681249-94-5 CAPLUS
CN Carbamic acid, [(1R)-3-[(8S)-8-[2-(dimethylamino)-2-oxoethyl]-5,6-dihydro-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



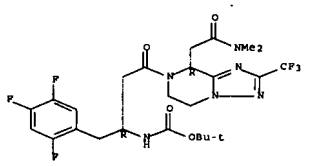
RN 681249-99-0 CAPLUS
CN Carbamic acid, [(1R)-3-[2-(difluoromethyl)-5,6-dihydro-5,8-dimethyl[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 681250-01-1 CAPLUS
CN Carbamic acid, [(1R)-3-[(8R)-8-[2-(dimethylamino)-2-oxoethyl]-5,6-dihydro-2-(trifluoromethyl)[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

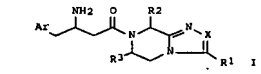
Absolute stereochemistry.

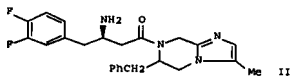


L11 ANSWER 110 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:796660 CAPLUS Full-text
DN 139:307796
TI Preparation of aminoacylimidazo- and triazolopyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes
IN Brockunier, Linda L.; Duffy, Joseph L.; Kim, Dooseop; Parmee, Emma R.; Weber, Ann E.
PA (Merck & Co., Inc., USA
SO PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003082817	A2	20031009	WO 2003-US8723	20030321
WO 2003082817	A3	20031218		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2478389	A1	20031009	CA 2003-2478389	20030321
AU 2003225916	A1	20031013	AU 2003-225916	20030321
EP 1490335	A2	20041229	EP 2003-745557	20030321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526811	T	20050908	JP 2003-580285	20030321
US 2005107390	A1	20050519	US 2004-508898	20040923

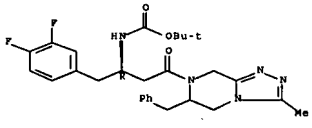
PRAI US 2002-367410P P 20020325
WO 2003-US8723 W 20030321
OS MARPAT 139:307796
GI



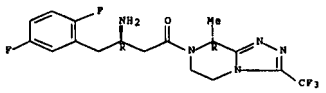


AB Title compds. I [Ar = (un)substituted Ph; X = N, (un)substituted CH2; R1 = H, CN, (un)substituted alkyl, Ph, heterocyclic; R2, R3 = H, CN, (un)substituted alkyl, Ph, naphthyl, CO2H, CONH2, cycloalkyl] were prepared for use as dipeptidyl peptidase-IV inhibitors in the treatment or prevention of diseases, such as diabetes and particularly type 2 diabetes. Thus, 6-benzyl-3-methyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine was prepared in 5 steps from 2-benzyloxirane and was acylated with (R)-3,4-F2C6H3CH2CH(NHCO2CMe3)CH2CO2H and deblocked to give the imidazopyrazine II.
IT 611240-63-2P 611240-81-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoacylimidazo- and triazolopyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes)
RN 611240-63-2 CAPLUS
CN Carbamic acid, [(1R)-1-[(3,4-difluorophenyl)methyl]-3-[5,6-dihydro-3-methyl-6-(phenylmethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

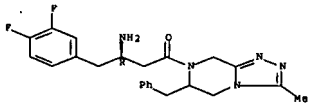


RN 611240-81-4 CAPLUS
CN Carbamic acid, [(1R)-3-[5,6-dihydro-8-methyl-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX



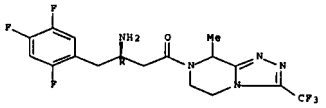
RN 611240-26-7 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-methyl-6-(phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



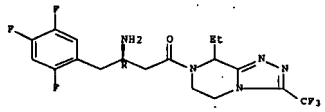
RN 611240-27-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-8-methyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



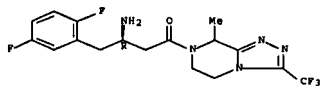
RN 611240-39-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-8-ethyl-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



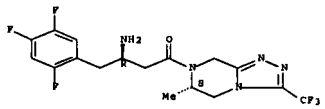
RN 611240-40-5 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-8-methyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



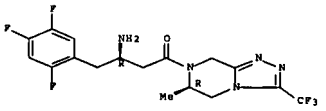
RN 611240-41-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-6-methyl-3-(trifluoromethyl)-, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



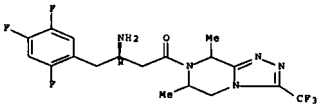
RN 611240-42-7 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-6-methyl-3-(trifluoromethyl)-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



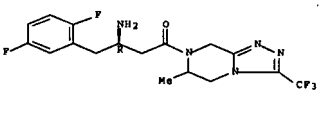
RN 611240-43-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-6,8-dimethyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



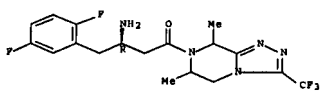
RN 611240-44-9 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-6-methyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 611240-45-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-6,8-dimethyl-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

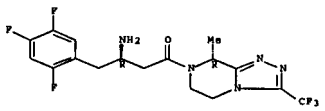


RN 611240-80-3 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-8-methyl-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, (8R)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 611240-79-0
CMF C17 H17 F6 N5 O

Absolute stereochemistry.

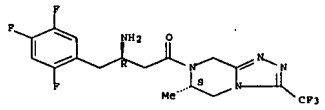


CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 611240-88-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-6-methyl-3-(trifluoromethyl)-, monohydrochloride, (6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L11 ANSWER 11 OF 111 CAPLUS COPYRIGHT 2007 ACS on STN
AN 2003:42275 CAPLUS Full-text
DN 138:106717
TI Preparation of β-amino tetrahydroimidazo[1,2-a]pyrazines and tetrahydrotrioazolo[4,3-a]pyrazines as dipeptidyl peptidase inhibitors for the treatment or prevention of diabetes
IN Edmondson, Scott D.; Fisher, Michael H.; Kim, Dooseop; MacCoss, Malcolm; Parmee, Emma R.; Weber, Ann E.; Xu, Jinyou
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003004498	A1	20030116	WO 2002-US21349	20020705
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2002320303	A1	20030121	AU 2002-320303	20020705
US 2003100563	A1	20030529	US 2002-189603	20020705
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HU 200401104	A2	20040928	HU 2004-1104	20020705
JP 2004536115	T	20041202	JP 2003-510665	20020705
JP 3762407	B2	20060405		
TW 226331	B	20050111	TW 2002-91114990	20020705
NZ 529833	A	20050128	NZ 2002-529833	20020705
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CN 1861077	A	20061115	CN 2006-10077691	20020705
ZA 2003009294	A	20040722	ZA 2003-9294	20031128
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IN 2004CN00026	A	20051202	IN 2004-CN26	20040106
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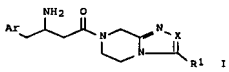
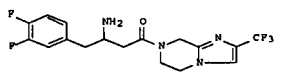
EP 2002-749813	A3	20020705		
WO 2002-US21349	W	20020705		
US 2003-481353	A1	20031219		

OS MARPAT 138:106717
GI



I



II

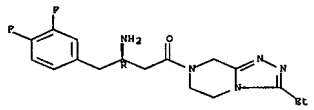
AB β-Amino tetrahydroimidazo[1,2-a]pyrazines and tetrahydrotrioazolo[4,3-a]pyrazines [e.g., I; wherein Ar = (substituted) phenyl; X = N, CR2; R1, R2, independently = H, CN, (branched) (substituted) (C1-C10)alkyl, (substituted) Ph, (saturated) 5- or 6-membered heterocycle, etc.] were prepared For example, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)butanoyl]-2- (trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine (II) was prepared in several steps. The prepared compds. are inhibitors of the dipeptidyl peptidase-IV enzyme (*DP-IV inhibitors*) and, thus, are useful in the treatment or prevention of diseases in which the dipeptidyl peptidase-IV enzyme is involved, such as type 2 diabetes (no data).

IT 486459-69-2P 486459-70-5P 486459-71-6P
486459-82-9P 486459-83-0P 486459-84-1P
486459-85-2P 486459-86-3P 486459-87-4P
486459-88-5P 486459-89-6P 486459-57-6P
486460-31-5P 486460-32-6P 487064-52-2P
487064-54-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of β-amino tetrahydroimidazo[1,2-a]pyrazines and tetrahydrotrioazolo[4,3-a]pyrazines as dipeptidyl peptidase inhibitors)

RN 486459-69-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro-, dihydrochloride (9CI) (CA INDEX NAME)

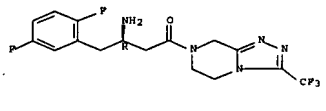
Absolute stereochemistry.



●2 HCl

RN 486459-70-5 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

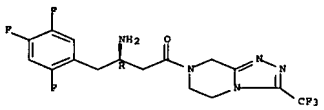
Absolute stereochemistry.



● HCl

RN 486459-71-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-, monohydrochloride (9CI) (CA INDEX NAME)

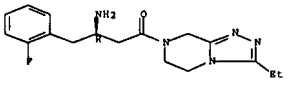
Absolute stereochemistry.



● HCl

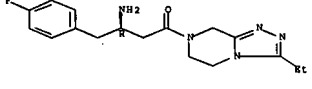
RN 486459-82-9 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2-fluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



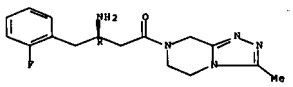
RN 486459-83-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



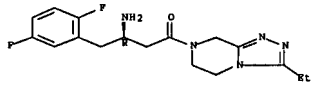
RN 486459-84-1 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2-fluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



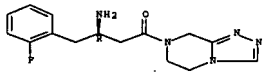
RN 486459-85-2 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-3-ethyl-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



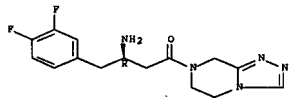
RN 486459-86-3 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2-fluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



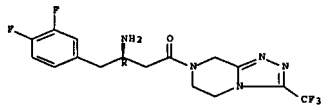
RN 486459-87-4 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



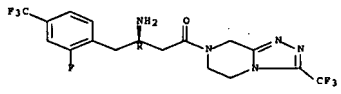
RN 486459-88-5 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



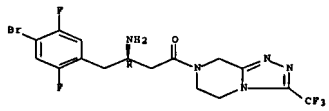
RN 486459-89-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-[2-fluoro-4-(trifluoromethyl)phenyl]-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



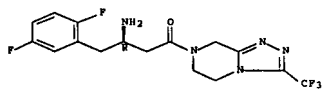
RN 486459-97-6 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(4-bromo-2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



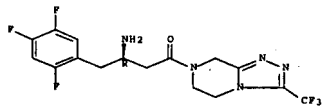
RN 486460-31-5 CAPLUS
CN 1-Butanone, 3-amino-4-(2,5-difluorophenyl)-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



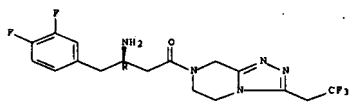
RN 486460-32-6 CAPLUS
CN 1-Butanone, 3-amino-1-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-4-(2,4,5-trifluorophenyl)-, (3R)- (CA INDEX NAME)

Absolute stereochemistry.



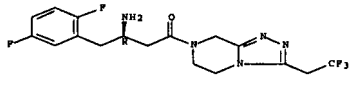
RN 487064-52-8 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(3,4-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



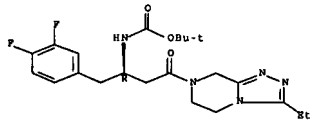
RN 487064-54-0 CAPLUS
CN 1,2,4-Triazolo[4,3-a]pyrazine, 7-[(3R)-3-amino-4-(2,5-difluorophenyl)-1-oxobutyl]-5,6,7,8-tetrahydro-3-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



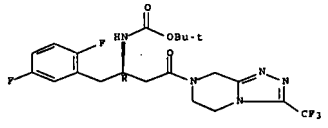
IT 486460-19-9P 486460-22-4P 486460-23-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of β-amino tetrahydroimidazo[1,2-a]pyrazines and tetrahydrotrioazolo[4,3-a]pyrazines as dipeptidyl peptidase inhibitors)
RN 486460-19-9 CAPLUS
CN Carbamic acid, [(1R)-1-[(3,4-difluorophenyl)methyl]-3-(3-ethyl-5,6-dihydro-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl)-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



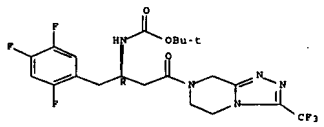
RN 486460-22-4 CAPLUS
CN Carbamic acid, [(1R)-1-[(2,5-difluorophenyl)methyl]-3-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 486460-23-5 CAPLUS
CN Carbamic acid, [(1R)-3-[5,6-dihydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazin-7(8H)-yl]-3-oxo-1-[(2,4,5-trifluorophenyl)methyl]propyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil stng

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	591.08	964.90

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-86.58	-87.36

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STN INTERNATIONAL LOGOFF AT 11:06:44 ON 08 AUG 2007